**UNITED STATES DISTRICT COURT**
**DISTRICT OF NEW JERSEY**

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| ORTHO-MCNEIL PHARMACEUTICAL, INC.,<br><br>Plaintiff and Counterclaim Defendant,<br><br>v.<br><br>KALI LABORATORIES, INC., PAR PHARMACEUTICAL COMPANIES, INC., PAR PHARMACEUTICAL, INC.,<br><br>Defendants and Counterclaimants. | CIVIL ACTION NO.: 02-5707 (JCL) |
| ORTHO-MCNEIL PHARMACEUTICAL, INC.,<br><br>Plaintiff and Counterclaim Defendant,<br><br>v.<br><br>TEVA PHARMACEUTICAL INDUSTRIES, LTD., TEVA PHARMACEUTICALS USA, INC., BARR LABORATORIES, INC.<br><br>Defendants and Counterclaimants. | CIVIL ACTION NO.: 04-0886 (JCL) (CLOSED)<br><br>**OPINION** |

**LIFLAND, District Judge**

In these two consolidated patent infringement actions, Defendant generic drug manufacturers Kali Laboratories, Inc. ("Kali"), Par Pharmaceutical Companies, Inc., Par Pharmaceutical, Inc. (collectively "Par"),[1] Teva Pharmaceutical Industries, Ltd., Teva Pharmaceuticals USA, Inc. (collectively "Teva"), and Barr Laboratories, Inc. ("Barr"),[2] move for summary judgment against Plaintiff Ortho-McNeil Pharmaceutical, Inc. ("Ortho-McNeil"). Ortho-McNeil asserts that Defendants have infringed, under the Hatch-Waxman Act, its patent covering the pain-relief drug it sells under the name-brand, Ultracet. Defendants dispute Ortho-McNeil's infringement claims, and counterclaim that, in any event, Ortho-McNeil's patent is invalid. For the reasons that follow, the Court will grant summary judgment of non-infringement to Kali, and deny summary

[1] Kali and Par are co-defendants in civil action no. 02-5707. Kali was initially the sole defendant, but on June 10, 2004, Par acquired Kali, and thereafter was joined as a defendant by Ortho-McNeil. For simplicity's sake, the Court will collectively refer to Defendants in No. 02-5707 as "Kali."

[2] Teva and Barr are co-defendants in civil action no. 04-0886. In January 2006, Teva transferred to Barr all right, title, and interest in its Abbreviated New Drug Application No. 76-914, which is the subject of Ortho-McNeil's suit. Thereafter, on March 8, 2006, Barr was joined as a defendant in the action, and Teva remained active in the liability phase of the case only for discovery purposes. (Stipulation and Order Regarding Teva's Motion to Substitute Barr, ¶ 3.) The Court will refer to each defendant in No. 04-0886 individually where appropriate, and jointly as "Teva/Barr" where appropriate.

judgment of non-infringement to Teva/Barr. Furthermore, the Court will grant summary judgment of infringement in favor of Ortho-McNeil against Teva/Barr. As for Defendants' invalidity counterclaims, the Court will deny summary judgment of invalidity to Kali on the grounds of indefiniteness and the public-use bar. However, the Court concludes that Claim 6 of the '691 patent is invalid for anticipation, and for obviousness, and thus, will grant summary judgment of invalidity to Teva/Barr and Kali.

## I. Background

### A. Ortho-McNeil's Patented Invention

United States Patent No. 5,336,691 ("the '691 patent") contains 15 claims, several of which disclose a pharmaceutical composition comprising the analgesic compounds tramadol and acetaminophen combined at various weight ratios. The '691 patent inventors found that when administered together, certain amounts of tramadol and acetaminophen exhibit "synergistic" effects. In other words, the analgesic effectiveness of the two drugs in combination is greater than the sum of their parts, as predicted by data demonstrating the individual effectiveness of each drug. Claim 6, the only claim Ortho-McNeil asserts as infringed, reads: "[A] pharmaceutical composition [comprising a tramadol material and acetaminophen, wherein the ratio of the tramadol material to acetaminophen is a weight ratio of]

about 1:5."[3] '691 patent, col. 11, ll. 18-34.

At first, the United States Patent and Trademark Office ("PTO") rejected the '691 patent's claims for obviousness in view of the patent covering tramadol, U.S. Patent No. 3,652,589 ("the '589 patent" or "the Flick patent"). (Kushan Decl., Ex. 10, at KAL 0016264.) The examiner pointed out that the Flick patent disclosed tramadol's "considerable therapeutic value when used in combination with other therapeutically active agents whereby frequently a synergistic effect is observed," and reasoned that it therefore would have been obvious to one of ordinary skill in the art to combine tramadol and acetaminophen in varying amounts to achieve synergistic effects in treating pain. (Kushan Decl., Ex. 10, at KAL 0016264 (quoting '589 patent, col. 12, ll. 45-48).)

After the inventors counterargued that it was not obvious that tramadol and acetaminophen would exhibit synergistic analgesic activity in the particular weight ratios claimed, the PTO allowed the claims. (Kushan Decl., Ex. 10, KAL016272.) The '691 patent issued on August 9, 1994 to co-inventors Robert Raffa and Jeffrey Vaught, and was assigned to McNeilab, Inc., Ortho-McNeil's predecessor in interest.

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[3] Claim 6 is dependent upon the limitations of Claims 1 and 5, and those limitations have been incorporated here into the language of Claim 6.

On the basis of the '691 patent, Ortho-McNeil developed Ultracet, which contains one part tramadol hydrochloride[4] (37.5 milligrams ("mg")), to 8.67 parts acetaminophen (325 mg). Ultracet was approved for sale by the Food and Drug Administration ("FDA") in 2001.

**B. Kali's and Teva/Barr's Abbreviated New Drug Applications**

In fall 2002, Kali filed an Abbreviated New Drug Application ("ANDA") with the FDA seeking approval to sell a generic version of Ultracet containing the identical 1:8.67 weight ratio of tramadol to acetaminophen. (Kushan Decl., Ex. 24.) Kali's ANDA included a certification under section 505(j)(2)(A)(vii)(IV) of the Federal Food and Drug Cosmetic Act ("FDCA"), 21 U.S.C. § 335 ("Paragraph IV certification"), alleging that the sale of its generic would either not infringe the '691 patent, or that the '691 patent was invalid, or both. Kali notified Ortho-McNeil of its Paragraph IV certification as required under 21 U.S.C. § 355(j)(2)(B), and Ortho-McNeil responded by filing an infringement suit against Kali under the Hatch-Waxman Act, 35 U.S.C. § 271(e)(2)(A). Kali denies infringing the '691 patent, and asserts, as affirmative defenses and in counterclaims, that the '691 patent is invalid as anticipated, for obviousness, for

[4] In this opinion, tramadol hydrochloride will be referred to as simply, "tramadol."

indefiniteness, and under the public-use bar. After discovery, Kali filed the instant motion for summary judgment. On April 22, 2005, the 30-month stay on FDA approval of Kali's ANDA expired, see 21 U.S.C. § 355(j)(5)(B)(iii)(I)-(III), the FDA approved the ANDA, and Kali began marketing its generic form of Ultracet.[5]

In a separate suit, Ortho-McNeil filed a Hatch-Waxman Act infringement action against Teva on February 25, 2004, after Teva filed an ANDA with a Paragraph IV certification seeking to market a generic form of Ultracet. Like Kali, Teva responded by denying infringement, and by asserting a counterclaim alleging the invalidity of Claim 6. Teva/Barr now move for summary judgment on those grounds. On July 26, 2006, Barr began marketing its Ultracet generic after the 30-month stay on FDA approval expired.[6]

On July 10, 2006, the two cases were consolidated for pretrial purposes.

**C. The '691 Patent Reissue Application**

On January 20, 2004, during the discovery phase of its suit against Kali, and

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[5] After Kali began selling its generic form of Ultracet, Ortho-McNeil amended its complaint to assert claims for actual infringement and damages in addition to its Hatch-Waxman Act claim. No motion has been filed with regard to the sales of Kali's generic product. Therefore, the current summary judgment motion pertains only to Ortho-McNeil's Hatch-Waxman Act claim.

[6] As it did in its suit against Kali, Ortho-McNeil amended its complaint against Teva/Barr to assert actual infringement after Barr began marketing its generic version of Ultracet.

about one month prior to filing suit against Teva/Barr, Ortho-McNeil filed a reissue application with the PTO for the '691 patent, admitting that certain claims were anticipated by the prior art. Ortho-McNeil explained to the PTO that "it was not appreciated, by the inventors and the attorney prosecuting the underlying patent application [for the '691 patent], that a composition within the scope of at least claim 1 as issued appears to have been disclosed in at least [the Flick patent]." (Brown Decl., Ex. 10, Reissue Appl. Decl. of Jan. 20, 2004.) The reissue application canceled all claims of the '691 patent, except for Claims 6 and 15, and applied for dozens of new claims.

On August 1, 2006, the PTO reissued the '691 patent as U.S. Reissue Patent No. RE39,221 E ("the RE221 patent"). The RE221 patent retains Claim 6, only now recast as an independent claim,[7] and adds 62 additional new claims.[8] As required by the FDCA, Ortho-McNeil surrendered the '691 patent to the PTO. Because Claim 6 of the RE221 patent is "substantially identical" to Claim 6 of the

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[7] Claim 6 of the RE221 patent reads: "A pharmaceutical composition comprising a tramadol material and acetaminophen, wherein the ratio of the tramadol material to acetaminophen is a weight ratio of about 1:5."

[8] In a separate action filed on October 4, 2006, and now pending before this Court, Ortho-McNeil alleges that Defendants have also infringed various of these newly reissued claims. See Ortho-McNeil Pharm. Inc. v. Kali Labs. Inc., No. 06-cv-3533 (JCL).

'691 patent, the surrender of the '691 patent does not abate the current action. See 35 U.S.C. § 252. Ortho-McNeil amended its complaints in both actions to allege that Defendants' ANDAs infringed Claim 6 of the RE221 patent, and Kali and Teva/Barr amended their counterclaims to allege the invalidity of Claim 6 of the RE221 patent.[9]

## II. Summary Judgment

Summary judgment is appropriate if there is no genuine issue as to any material fact and the moving party is entitled to a judgment as a matter of law. Fed. R. Civ. P. 56; Serbin v. Bora Corp., 96 F.3d 66, 69 n.2 (3d Cir. 1996). When evaluating a summary judgment motion, the Court must "draw all reasonable inferences in favor of the non-moving party." Armour v. County of Beaver, 271 F.3d 417, 420 (3d Cir. 2001) (internal quotations omitted). The burden of showing that no genuine issue of material fact exists rests initially on the moving party. Celotex Corp. v. Catrett, 477 U.S. 317, 323 (1986); Huang v. BP Amoco Corp., 271 F.3d 560, 564 (3d Cir. 2001). Once the moving party has made a properly supported motion for summary judgment, the burden shifts to the non-

[9] Because Claim 6 and the relevant portions of the specification remain substantially unchanged in the RE221 patent, the Court will continue to refer to the patent at issue as the '691 patent, except where the context requires otherwise. Cf. Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs, Ltd., 476 F.3d 1321, No. 06-1102, 2007 U.S. App. LEXIS 1133, at *8 n.3 (Fed. Cir. Jan. 19, 2007).

moving party to "set forth specific facts showing that there is a genuine issue for trial." Fed. R. Civ. P. 56(e); Anderson, 477 U.S. at 242.

The mere existence of some alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment. Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 586 (1986); Quiroga v. Hasbro, Inc., 934 F.2d 497, 500 (3d Cir. 1991) (noting that a motion for summary judgment is not defeated by mere allegations, general denials, or other "vague statements"). Rather, only disputes regarding facts that might affect the outcome of the lawsuit under the governing law will preclude the entry of summary judgment. Anderson, 477 U.S. at 247-48. If the evidence is "such that a reasonable jury could return a verdict for the nonmoving party," summary judgment should not be granted. Id. at 248; Lawrence v. Nat'l Westminster Bank of New Jersey, 98 F.3d 61, 65 (3d Cir. 1996).

## III. Discussion

Kali and Teva/Barr claim that, as a matter of law, Ortho-McNeil has failed to carry its burden of proving infringement, and that they have carried their burden of proving the invalidity of the '691 patent on grounds of anticipation. Kali also seeks summary judgment on its additional invalidity counterclaims of indefiniteness, obviousness, and the public-use bar. The Court's first step in

evaluating Defendants' motions is to objectively construe the disputed limitations of Claim 6 to the extent necessary to settle the controversy, and without reference to Defendants' allegedly infringing products. See Vivid Techs., Inc. v. American Science & Eng'g, Inc., 200 F.3d 795, 803 (Fed. Cir. 1999).

**A. Claim Construction**

"[T]he claims of a patent define the invention to which the patentee is entitled the right to exclude," Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed Cir. 2005) (internal quotations omitted), and therefore an interpretation of the words of those claims is necessary in order to determine whether the invention is infringed, or invalid, see, e.g., Lemelson v. Gen. Mills, Inc., 968 F.2d 1202, 1206 (Fed. Cir. 1992) ("It is elementary in patent law that, in determining whether a patent is valid and, if valid, infringed, the first step is to determine the meaning and scope of each claim in suit."). The proper construction of a disputed claim limitation is decided by the Court as a matter of law, Bayer AG v. Elan Pharm. Research Corp., 212 F.3d 1241, 1247 (Fed. Cir. 2000), and is applicable to both the Court's infringement and invalidity analyses, Amazon.com, Inc. v. Barnesandnoble.com, Inc., 239 F.3d 1343, 1351 (Fed. Cir. 2001).

The Court of Appeals for the Federal Circuit has repeatedly stated that "the words of a claim 'are generally given their ordinary and customary meaning,'" as

viewed through the eyes of "a person of ordinary skill in the art in question at the time of the invention." Phillips, 415 F.3d at 1312-13 (quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed Cir. 1996)). In some cases, the ordinary and customary meaning of a limitation may be "readily apparent even to lay judges," and thus, can be simply applied to a claim with the assistance of a dictionary. Id. at 1314. In most cases, however, the "meaning of a claim term as understood by persons of skill in the art is . . . not immediately apparent," and therefore the court must look to "'those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean.'" Id. (quoting Innova/Pure Water, Inc. v. Safari Water Filtration Systems, Inc., 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

"[T]hose sources" can be divided into two general categories: intrinsic evidence and extrinsic evidence. Intrinsic evidence consists of the words of the claims themselves, the specification, and, if in evidence, the prosecution history. Key Pharms. v. Hercon Lab. Corp., 161 F.3d 709, 716 (Fed. Cir. 1998). Extrinsic evidence consists of any evidence outside of the patent record, id., such as, "expert and inventor testimony, dictionaries, and learned treatises," Markman v. Westview Instruments, Inc., 52 F.3d 967, 980 (Fed. Cir. 1995), aff'd, 516 U.S. 370 (1996). Such evidence "may be helpful to explain scientific principles, the meaning of

technical terms, and the terms of art that appear in the patent and prosecution history"–in a nutshell, extrinsic evidence "'aid[s] the court in the construction of the patent.'" Id. The Federal Circuit has stressed, however, that intrinsic evidence has primacy in the claim construction analysis; extrinsic evidence cannot be used to alter a construction of the claims mandated by the intrinsic evidence. Key Pharms, 161 F.3d at 716. "[I]f the meaning of a disputed claim term is clear from the intrinsic evidence . . . that meaning, and no other, must prevail." Id.

Despite the, at times, seemingly factual nature of this exercise,[10] claim construction is purely a question of law. "Testimony about construction . . . amounts to no more than legal opinion," which the "court has complete discretion to" wholly adopt, use as guidance, ignore or exclude. Markman, 52 F.3d at 983. As a result, conflicts between expert testimony or between testimony and the intrinsic evidence does not create a question of fact that can preclude summary judgment. See id.

As stated above, Claim 6 of the '691 patent reads: "[A] pharmaceutical composition [comprising a tramadol material and acetaminophen, wherein the ratio of the tramadol material to acetaminophen is a weight ratio of] about 1:5."

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[10] See, e.g., Cybor Corp. v. FAS Techs., 138 F.3d 1448, 1475 (Fed Cir. 1998) (Rader, J., dissenting).

'691 patent, col. 11, ll. 18-34. The parties dispute the meaning of the limitations "about 1:5" and "pharmaceutical composition." The Court will construe each in turn.

### 1. "About 1:5"

#### a. The Parties' Positions

It is undisputed that, at a minimum, "about 1:5" is equivalent to "approximately 1:5," and therefore permits some amount of deviation from exactly 1:5. The parties' positions diverge, however, as to the amount of deviation "about" permits. Ortho-McNeil argues that "about 1:5" should encompass at least 1:3.6 to 1:7.1, because, in terms of efficacy, the ratios in this range are statistically equivalent to 1:5. Kali and Teva/Barr counter that "about" should only encompass minor deviations from 1:5 resulting from "measurement error," and that this range should span, at most, from 1:4.9 to 1:5.1. Before the Court examines the intrinsic and extrinsic evidence, two preliminary issues must first be addressed.

#### b. The Effect of the Federal Circuit's Decision in Ortho-McNeil v. Caraco

On January 19, 2007, the Court of Appeals for the Federal Circuit issued a decision construing the "about 1:5" limitation in Claim 6 of the '691 patent in a nearly identical Hatch-Waxman Act infringement case brought by Ortho-McNeil

against another generic drug manufacturer. See Ortho-McNeil Pharm., Inc. v. Caraco Pharm. Labs, Ltd., 476 F.3d 1321, 2007 U.S. App. LEXIS 1133 (Fed. Cir. Jan. 19, 2007). There, the Federal Circuit held that the District Court for the Eastern District of Michigan properly interpreted "about 1:5" to mean "approximately 1:5, encompassing a range of ratios no greater than 1:3.6 to 1:7.1." Id. at *18-19.

Ortho-McNeil argues that this holding settles the claim construction dispute in this case, and definitively sets "about 1:5" as equal to 1:3.6 to 1:7.1. The Court disagrees. The facts and analysis of Caraco make clear that the Federal Circuit was not deciding the exact parameters of "about 1:5," but instead was only placing a ceiling on what range of ratios "about" could possibly represent. In Caraco, the defendant generic manufacturer's ANDA would have permitted it to sell a generic Ultracet with a weight ratio of 1:8.67; however, the ANDA also included a manufacturing variance that would have allowed the defendant to legally sell its generic with a weight ratio ranging as low[11] as 1:6.41. See Ortho-McNeil Pharm. Inc. v. Caraco Pharm. Labs., Ltd., No. 04-CV-73698, 2005 U.S. Dist. LEXIS

[11] As the Federal Circuit did in Caraco, the Court here will use terminology that compares different ratios in terms of their second number. For example, even though the fraction 1:6.41 is greater than 1:8.67, the Court will call it "lesser" or "lower," because 6.41 is less than 8.67.

24998, at *2 (E.D. Mich. Oct. 19, 2005). Ortho-McNeil argued there, as it does here, that "about 1:5" encompasses at least 1:3.6 to 1:7.1, the range of ratios representing the statistical variation in efficacy of 1:5. Id. at *7-8. However, during the litigation, the defendant amended its ANDA to "cut its authorized manufacturing variability in half to a minimum of 1:7.5." Id. at *2-3. Thus, under the facts presented in Caraco, the Federal Circuit only needed to decide whether "about 1:5" could extend *higher* than 1:7.1, as urged in that case by Ortho-McNeil,[12] in order to determine whether there was literal infringement. Absent language in Caraco to the contrary, this Court will not assume that the Federal Circuit decided more. See NTP, Inc. v. Research in Motion, Ltd., 418 F.3d 1282, 1311 (Fed Cir. 2005) (stating that a court need only construe a claim term "to the extent necessary to resolve the controversy") (quoting Vivd Techs., Inc., 200 F.3d at 803); see also Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1219 (Fed. Cir. 1995) (construing "about 5:1" to "not include the [allegedly infringing] ratio of 4:1," without determining exactly how far "about" expands 5:1).

The Federal Circuit's analysis also indicates that it only decided whether the

[12] See Caraco, 2005 U.S. Dist. LEXIS 24998, at *8 (describing how Ortho-McNeil argued before the District Court that the scope of "'about 1:5' necessarily extends somewhat beyond" 1:3.6 to 1.7.1, in an apparent attempt to encompass the 1:7.5 floor set by the defendant's amended ANDA).

scope of "about 1:5" was broader, not equal to or narrower, than 1:3.6 to 1:7.1. First, Caraco simply held that "about 1:5" was "no greater" than 1:3.6 to 1:7.1, rather than using language indicating an equivalence to this range, such as "extends to" or "no greater *and no lesser than*." Second, Caraco's claim construction stressed that "the qualifier 'about' is *narrow*," and that it "was meant to encompass compositions *very close* to" 1:5, Caraco, 2007 U.S. App. LEXIS 1133, at *16-17 (emphases added), thus indicating that the Court was only concerned with whether the scope of "about 1:5" was broader than 1:3.6 to 1:7.1. Third, the Federal Circuit in Caraco never considered the defendant's argument there (and Defendants' argument in this case) that "about 1:5" should be construed more narrowly than 1:3.6 to 1:7.1 using measurement error. See Caraco, 2007 U.S. App. LEXIS 1133, at *5.

Finally, although the Caraco Court did rely in part on the opinion of Ortho-McNeil's expert, Donald R. Stanski, M.D., that "'about 1:5' . . . includes a ratio *up to and including* 1:7.1," Caraco, 2007 U.S. App. LEXIS 1133, at *18-19 (emphasis added), it did so only to undercut Ortho-McNeil's argument that "about 1:5" extends *beyond* 1:7.1, not to definitively state that "about 1:5" is equivalent to the full scope of 1:3.6 to 1:7.1. This is clearly how the District Court used Dr. Stanski's testimony in its analysis, when it explained that the "'[u]p to' 1:7.1,"

language Dr. Stanski used "would put an upper limit on the range, while [Ortho-McNeil's argument for] 'at least' 1:3.6 to 1:7.1 has no upper limit," and would "result[] in a meaningless and boundless construction." Caraco, 2005, U.S. Dist. LEXIS 24998, at *8-9. The Federal Circuit said that it "s[aw] no error in the district court's construction," and cited it approvingly. Caraco, 2007 U.S. App. LEXIS 1133, at *18.

The Court concludes that Caraco's holding that "about 1:5" extends "no greater than 1:3.6 to 1:7.1" did not answer whether the scope of "about 1:5" extends to a range narrower than 1:3.6 to 1:7.1. As a result Caraco does not settle the infringement issue here since Defendants' ANDAs would also permit them to legally sell their generic drug with a weight ratio as low as 1:6.41, and Defendants' have not voluntarily amended their ANDAs to limit this range. Thus, the Court must decide whether the meaning of "about 1:5" encompasses 1:6.41. This is the question the Court will address below.

**c. Construing the Term "About"**

The second preliminary issue the Court must address is Kali and Teva/Barr's suggestion that courts unvaryingly "interpret 'about' based on the imprecision inherent in measurement of the claimed element in question," (see, e.g., Kali Reply Br. at 7), and that therefore, this Court should do the same.

Not surprisingly, the proper interpretation of the word "about," when used in front of a numerical measurement in a patent claim, has been the subject of relatively frequent litigation before the Courts. See, e.g., Caraco, 2007 U.S. LEXIS 1133, at *18-19 (construing "about 1:5"); Merck, 395 F.3d at 1370 (interpreting "about 70 mg"); Pall, 66 F.3d at 1217-18 (interpreting "about 5:1 to about 7:1"); Hybritech, Inc. v. Abbott Labs., 849 F.2d 1446, 1455-56 (Fed Cir. 1988) (construing "about 10<8> liters/mole"); W.L. Gore & Assoc. Inc. v. Garlock, Inc., 842 F.2d 1275, 1280 (Fed. Cir. 1988) (construing "about 100% per second"). In support of their position, Kali and Teva/Barr cite Hybritech Inc. v. Abbott Laboratories, where the Federal Circuit, with little elaboration, affirmed a district court's construction of a claim requiring antibodies with an affinity of "at least about 10<8> liters/mole," as encompassing "two- to three-fold measurement errors inherent in affinity measurements." 849 F.2d at 1455.

The Federal Circuit has explained that "'the word 'about' does not have a universal meaning in patent claims, [and instead,] the meaning depends on the technological facts of the particular case.'" Caraco, 2007 U.S. App. LEXIS 1133, at *13 (quoting Pall, 66 F.3d at 1217). Therefore, the limitation "about" is not exempt from the Federal Circuit's instruction that the meaning of a claim limitation must be that which would be usual and customary to the person of

ordinary skill *in the particular art* at the time of *the particular invention*. See Phillips, 415 F.3d at 1312-13. Presumably, the Federal Circuit used this same context-specific approach in Hybritech, and, on the basis of intrinsic and extrinsic evidence relevant to that particular invention, concluded that measurement error was the appropriate benchmark for defining "about." See Hybritech, 849 F.2d at 1455. In other cases, involving different technologies, claims, and specifications, "about" may mean something different. For instance, in Pall, the Federal Circuit construed "about 5:1" not to encompass a ratio of 4:1 because test data in the patent specification and testimony of the inventor showed that a nylon resin membrane with a methylene to amide ratio of 4:1 lacked the desirable properties present in the claimed 5:1 ratio. Id. at 1217-18. In other words, the extent of "about" was limited by what worked as well as 5:1. Thus, the Court rejects Defendants' suggestion that Hybritech created a *per se* rule that "about" is always consistent with "measurement error." The meaning of "about 1:5" is dictated primarily by the intrinsic evidence in this case, to which the Court now turns.

**d. The Intrinsic Evidence**

**i. The '691 Patent Claims**

The claims of the '691 patent provide the starting point for an examination of the intrinsic evidence. See Phillips, 415 F.3d at 1314. Those claims make clear

that "about 1:5" was intended to be relatively narrow in scope because it is "distinctly claimed and distinguished from other broader weight ratio ranges in the patent," such as Claim 1 which contains the limitation: "a weight ratio from about 1:1 to about 1:1600." Caraco, 2007 U.S. App. LEXIS 1133, at *14-15. Besides Claim 6, only Claim 4, which claims "about 1:1," distinctly claims a single ratio as opposed to a range. Noting this, the Federal Circuit observed in Caraco that this is further evidence that "about" must be "narrow" because otherwise the scope of "about 1:5" would "encompass a range of ratios that could potentially render meaningless" the "about 1:1" limitation. Id. at *16-17.

Kali and Teva/Barr argue that the words of the claims support their measurement-error theory of claim construction. Defendants' position is that because the word "about" in the claim describes a weight ratio, "about" must be referring to imprecision in the measurement of the weights of tramadol and acetaminophen. Defendants argue further that, in contrast, Ortho-McNeil's claim construction theory (explained in detail below) is not supported by the words of the claims because it is based on animal testing data that does not appear in the claims.

Defendants are correct that the words of the claims do not refer to the test data, found in the specification, upon which Ortho-McNeil relies. But the claims

also do not refer to errors in the measurement of the weights of tramadol and/or acetaminophen. There are two gaps in Defendants' position. First, the fact that "about" modifies weight ratios only informs the reader that some degree of variation in those ratios is permitted. The language says nothing about what standard shall determine the correct degree of that variation, and therefore makes it no more likely that the inventors intended that variation to reflect errors in measuring the weight of tramadol or acetaminophen as opposed to the statistical imprecision inherent in the method of using the specification's test data to find efficacy at that ratio, as urged by Ortho-McNeil. Both could cause variation in the weight ratios, and the words of the claims are silent as to both.

Second, imprecision in a weight *ratio* is not the same thing as imprecision in a measurement of the weight of the drugs that constitute that ratio. A measuring error will not always cause imprecision or variation in the corresponding weight ratio. If a scientist intended to create a drug with a 1:5 weight ratio containing 25 mg of tramadol and 125 mg of acetaminophen, but mistakenly measured 30 mg of tramadol and 150 mg of acetaminophen, the scientist still would have created a drug with precisely a 1:5 weight ratio. While such an error may be unlikely, its possibility illustrates that using "about" to describe a weight *ratio* does not necessarily refer to errors in measuring the *weights* of the drugs constituting that

ratio.

In sum, the fact that "about" modifies weight ratios does not support Defendants' measurement error argument. It simply begs the question: what standard shall give meaning to the word "about"? Because the words of the claims do not answer this question, the Court will move on and examine the patent specification.

### ii. The Specification

The Federal Circuit has described the patent specification as "the single best guide to the meaning of a disputed term." See Vitronics, 90 F.3d at 1582. It "acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication." Id. (citing Markman, 52 F.3d at 979). The '691 patent specification does not explicitly define "about." Implicitly, however, the specification (1) supports a definition of "about" that encompasses the full extent of the variation inherent in the statistical method of determining whether tramadol/acetaminophen doses in certain weight ratios demonstrate efficacy, and (2) is wholly lacking in support for a definition linked to measurement error.

#### (a) Statistical Variation in Efficacy

According to the specification, the inventors only claimed weight ratios of

tramadol and acetaminophen that demonstrated synergistic effects when administered to test mice. '691 patent, col. 2, ll. 55-67; col. 3, l. 63-col. 4, l. 6; col 8 ll. 38-68. The specification also explains how the testing was performed and charts the resulting data. The mice were administered precise doses of tramadol and acetaminophen in each weight ratio tested, for example, 1000:1, 1:1, 1:5, and 1:5.7. Each weight ratio was tested using different dosages of the drugs. For example, the mice received the drugs at a 1:5 weight ratio in three ways: (1) 2.5 mg of tramadol and 12.5 mg of acetaminophen; (2) 5 mg of tramadol and 20 mg of acetaminophen; and (3) 10 mg of tramadol and 50 mg of acetaminophen. At each dosage, the inventors recorded what number out of 30 test mice experienced pain relief. See '691 patent, cols. 9-10.

Using the resulting data, the inventors then statistically estimated how many milligrams of tramadol and acetaminophen must be administered in order for 50 percent of the 30 test mice to experience pain relief at each particular weight ratio. The resulting value is called the "median effective dose" of the weight ratio, or "ED50" for short. See '691 patent, col. 8 ll. 29-30 (explaining that the "ED50 [value] was *estimated* from the dose-response curve for a specific fixed-ratio"

(emphasis added)); (Smith Inf. Rep., at pp. 8-9, ¶¶ 1-5.).[13] To illustrate, at 1:5, the test data found that 2.5 mg of tramadol and 12.5 mg of acetaminophen caused seven of 30 mice to experience pain relief; at 5 mg/25 mg, 18[14] of 30 mice experienced pain relief; and at 10 mg/50 mg, all 30 mice experienced pain relief. '691 patent, cols. 9-10, Table 1. Using that data, the inventors "estimated" that in order for 50 percent of 30 test mice to experience pain relief, it would be necessary to administer 4 mg of tramadol and 19.8 mg of acetaminophen. See '691 patent, col. 8 ll. 29-30; cols. 9-10. Therefore, 4 mg/19.8 mg is the ED50 for tramadol/acetaminophen at a 1:5 weight ratio. The ED50 data points for each weight ratio tested by the inventors are plotted in a graph found at Figure 1 of the specification.

Importantly, each ED50 value is only a statistical estimate, based upon the experimental data, of what the *true* ED50 value would be if it were possible to test

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[13] The Court finds the expert opinions of Dr. Stanski and Dr. Eric Smith helpful and persuasive in explaining some of the principles and terms of art appearing in the specification, and will rely on those opinions during its evaluation of the intrinsic evidence herein. See Markman, 52 F.3d at 980.

[14] Although the specification states that only 8 out of the 30 mice experienced pain relief at this level, Dr. Stanski's and Dr. Smith's expert reports state that this number should be 18 based on their calculations, and based on the calculations the inventors performed for each of the other ratios. They therefore conclude that the "8" must be a typographical error. (See Stanski Inf. Rep., at p. 6, ¶ 8; Smith Inf. Rep., at p. 7, ¶ 10.)

an *infinite* number of animals at a particular dose. (See Smith Inf. Rep., at pp. 4-5, ¶¶ 2-4.) Obviously, only a finite number of mice can be tested, here 30. If further experiments were conducted, the result would be "a slightly different proportion of animals testing 'positive' or 'negative,'" for pain relief, and thus, the ED50 value estimated from those results would also vary. (See id., at p. 5, ¶ 4.) To represent this uncertainty, Table 1 lists, and Figure 1 plots, the "95 percent confidence interval" of each weight ratio's ED50 values. '691 patent, Figure 1; col. 8, ll. 61-64; Table 1, cols. 9-10. "A confidence interval describes the variation in the estimate by using upper and lower values that represent a possible range of values that could be obtained from repeated experiments." (Smith Inf. Rep., at p. 5, ¶ 4.) Therefore, a 95 percent confidence interval means that if the inventors' mice experiment was repeated 100 times, roughly 95 percent of results would fall within the 95 percent confidence interval ranges. (Id. at p. 5, ¶ 4.)

The 95 percent confidence intervals for the 1:5 weight ratio's ED50 value (4.0 mg tramadol/19.8 mg acetaminophen) are 3.3 mg to 4.7 mg of tramadol, and 16.7 mg to 23.4 mg of acetaminophen. According to Ortho-McNeil's experts, Dr. Stanski, and Eric Smith, Ph.D., a range of weight ratios that are "statistically indistinguishable" from 1:5 can be discerned from these 95 percent confidence interval figures. (Smith Inf. Rep., at pp. 24-25, ¶¶ 1-3; Stanski Inf. Rep., at pp. 5-

7, ¶¶ 7, 10, 12.) The low end of the ratio range is determined by combining the lowest acetaminophen weight, 16.7 mg, with the highest tramadol weight, 4.7 mg. This combination results in a weight ratio of 1:3.6. The high end is then determined by combining the highest acetaminophen weight, 23.4 mg, with the lowest tramadol weight, 3.3 mg. This results in a weight ratio of 1:7.1. Thus, in Dr. Stanski's and Dr. Smith's opinions, the data in the specification demonstrates that a 1:5 weight ratio is statistically indistinguishable from a range of 1:3.6 to 1:7.1. (Smith Inf. Rep., at p. 24, ¶ 1[15]; Stanski Inf. Rep., at p. 6, ¶ 7; p. 7, ¶ 10, 12.) A person of skill in the art of analgesic drugs reading this data would find, Dr. Stanski concludes, that "about" encompasses this "statistical variation in efficacy" of the 1:5 weight ratio, and therefore, "'about 1:5' would not be statistically different from a ratio *up to and including* 1:7.1 and a ratio *down to and including* 1:3.6." (Stanski Inf. Rep., at p. 6, ¶ 7; p. 7, ¶ 12 (emphases added).)

Defendants seek to discredit Ortho-McNeil's theory of claim construction as mere manufactured "statistical machinations" (Kali Supp. Br. at p. 10.), and "statistical gymnastics," (Teva/Barr Reply Br. at p. 2.). However, Ortho-McNeil's expert states that the methodology used by the inventors is not novel in the

[15] Dr. Smith's report actually claims that 1:3.55 to 1:7.09 is encompassed by "about 1:5." Dr. Stanski explained in his report that this only differs from his own 1:3.6 to 1:7.1 range because he chose to round to the first decimal place.

pharmaceutical industry. (Smith Inf. Rep., at p. 8, ¶ 3.) Defendants do not offer extrinsic evidence to the contrary, and as explained further below, do not offer a more persuasive reading of the intrinsic evidence. Despite the use of data and statistics, Plaintiff's claim construction theory is not as complicated as Defendants would have it seem: the patent teaches that the inventors claimed 1:5 because it demonstrated efficacy, and, according to Plaintiff's experts, the patent data proving 1:5's efficacy also shows that the ratios 1:3.6 through 1:7.1 would, statistically speaking, demonstrate the same efficacy as 1:5. Thus, the Court concludes that this range of ratios offers a sound basis, grounded in the patent specification, for measuring the full breadth of "about 1:5." In contrast, Defendants have failed to show any reason, supported by the patent specification or otherwise, why "about" was intended to represent variation caused by measurement error.

**(b) Measurement Error**

Measurement error is not mentioned in any manner in the specification. This omission is significant, in light of the fact that the specification carefully details how the inventors prepared the tramadol/acetaminophen combinations administered to mice for testing. See '691 patent, col. 5, ll. 39-61; col. 6, ll. 32-52. If the occurrence of measurement errors were important enough, or common

enough, that the inventors felt the need to represent the variation created by such errors with the word "about" in the patent claims, one would think such errors would be accounted for in the specification's description of how the drug is prepared and measured for administration. Instead, the specification's description uses *precise* measurements. For example, in describing how the drugs at a 1:50 ratio were prepared, the specification states that

> 400 mg of [acetaminophen] as the free base is suspended with 10 mL of the 8 mg tramadol solution and 2 drops of TWEEN 80, a pharmacological dispersant, manufactured by Fisher Scientific Company, to yield the 1:50 ratio, i.e., (8 mg: 400 mg) combination per 10 mL of water.

'691 patent, col. 5, ll. 54-59. There is no mention of any variation in the amounts of tramadol or acetaminophen administered to the mice, with the word "about" or otherwise. Indeed, as Kali and Teva/Barr point out, the specification demonstrates that the inventors were capable of measuring the weight of the drugs with accuracy up to at least a hundred-thousandth of a milligram. See '691 patent, cols. 9-10 (stating that, at a weight ratio of 1:800, the inventors administered 0.03125 mg of tramadol to the test mice). Defendants argue that this precision proves that "about" should at most represent a one-tenth of decimal point variation from 1:5, i.e., 1:4.9 to 1:5.1. However, this argument prematurely assumes that measurement error has already been established as the guidepost for measuring the

variation represented by "about." It has not. Moreover, it also assumes that measurement errors are made. Simply because the data shows that the inventors could accurately measure tramadol to the fifth decimal place, in no way suggests that the inventors could not also do so to the sixth, seventh, or twentieth decimal places. Instead of proving that minute measurement errors should guide the meaning of "about," the precision measurements shown in the specification suggest that there were no imprecisions at all in weights of the drugs administered to the test rats. Even if measurement errors are made, the absence of any reference to them in the specification suggests that such errors were not contemplated by the inventors. As a result, a person of ordinary skill reading the patent would not contemplate that "about 1:5" refers to imprecision resulting from measurement errors.

Kali and Teva/Barr point out that the specification states that, in addition to testing tramadol and acetaminophen at a 1:5 weight ratio, the inventors also tested a 1:5.7 weight ratio. From this, Defendants argue that "about 1:5" cannot extend to 1:5.7 because the inventors recognized 1:5.7 and 1:5 as distinct ratios. This argument overlooks that, unlike the '691 patent's *claims*, the specification's test data does not use the word "about" before its tested ratios. Therefore, the specification does not show that "*about* 1:5" in Claim 6 does not encompass 1:5.7;

it only shows that the inventors considered *exactly* 1:5 to be distinct from *exactly* 1:5.7 for testing purposes. Furthermore, the fact that 1:5.7 was tested and ultimately *not claimed*, if anything, could suggest that the inventors thought that "*about* 1:5" already encompassed 1:5.7, and that therefore it was unnecessary to separately claim this data point. This is especially so in light of the test data, which shows that the 95 percent confidence intervals for the ED50 values of 1:5 (3.3-4.7 mg tramadol / 16.7-23.4 mg acetaminophen) encompass the ED50 values for 1:5.7 (4.1 mg tramadol / 23.3 mg acetaminophen). '691 patent, cols. 9-10, Table 1. Thus, Defendants' argument based on testing at a ratio of 1:5.7 further supports Ortho-McNeil's construction of "about 1:5."

In conclusion, the Court finds no basis in the intrinsic[16] or extrinsic evidence for using measurement error as a guide for construing the scope of "about 1:5." In contrast, the Court finds that the statistical variation in efficacy provides an appropriate benchmark. As explained above, the Federal Circuit in Caraco used this standard to set a ceiling for "about 1:5." This Court finds that it provides a floor as well, and holds that "about 1:5" encompasses ratios up to and including 1:7.1 and ratios down to and including 1:3.6.

[16] Neither party argues that the prosecution history of the '691 patent sheds light on the proper interpretation of "about 1:5."

### 2. "Pharmaceutical Composition"

Ortho-McNeil and Kali[17] also disagree over the proper construction of the Claim 6 limitation: "*pharmaceutical composition* [comprising a tramadol material and acetaminophen]." (emphasis added). Kali argues that the co-administration of tramadol and acetaminophen in separate but concurrent or sequential doses qualifies as a "pharmaceutical composition." Ortho-McNeil counterargues that the term is limited to "a medicinal preparation comprising an 'intimate admixture' of " tramadol and acetaminophen, "prepared outside the body, generally in the form of a 'dosage unit' such as a 'tablet' or 'capsule.'" (Pl.'s Opp. Br., p. 27.) The Court concludes that the intrinsic evidence favors Ortho-McNeil's construction.

The specification describes "[p]harmaceutical compositions comprising the tramadol material and acetaminophen," as "an intimate admixture with a pharmaceutical carrier . . . ." '691 patent, col. 4, ll. 42-45. The pharmaceutical carrier can take various forms, such as water, alcohols, starches, or sugars, depending on whether the composition is to be administered orally, intravenously, or parenterally. Id. at ll. 47-49, 53-59. The specification further explains that the "pharmaceutical compositions will generally be in the form of a dosage unit, e.g.,

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[17] For purposes of their summary judgment motion, Teva/Barr do not challenge Ortho-McNeil's construction of "pharmaceutical composition."

tablet, capsule, powder, injection, teaspoonful and the like," and that this dosage unit will "contain[] . . . preferably from about 0.3 to 200 mg/kg *of the active ingredients*," id. at col. 5, ll. 3-7 (emphasis added). Therefore, a "pharmaceutical composition" necessarily contains both tramadol and acetaminophen. Additionally, examples one, two, and three of the specification, which give instructions on the "Preparation of the Combined Doses of Tramadol and [acetaminophen]," all state that the tramadol/acetaminophen "combinations are . . . made by adding 10 mL of each [tramadol] dilution to the appropriate mg of [acetaminophen]." '691 patent, col. 5, ll. 38-53; col. 6, ll. 32-44; col. 7, ll. 23-36. Thus, the specification makes clear that a pharmaceutical composition was intended to be a single dosage unit containing a mixture of both active ingredients.

The prosecution history also supports this construction. In an April 2, 1993 letter, the PTO informed the inventors that their claims had been rejected as obvious over the Flick patent, because "it would have been obvious to one with ordinary skill in the art *to combine two compounds* (i.e. tramadol and acetaminophen) in varying amounts *in the same composition* since both compounds are known to useful (sic) for treating the same condition (i.e. pain)." (Kushan Decl., Ex. 10, at KAL016264 (emphases added).) Thus, it is apparent that the patent examiner understood "pharmaceutical composition" to require the

combination of the two compounds in the same unit. In its response, Ortho-McNeil did not attempt to change the examiner's understanding of the invention. (Kushan Decl., Ex. 10, at KAL016271-73.)

Ortho-McNeil also presents extrinsic evidence supporting its construction. First, in the expert opinion of Dr. Stanski, based on how the phrase is "commonly used in medical terminology, a pharmaceutical composition of Tramadol and [acetaminophen] would not extend to tablets in which the Tramadol and the [acetaminophen] were not in an 'intimate admixture' (e.g., two tablets, one solely containing tramadol and one solely containing [acetaminophen])." (Stanski Inf. Rep., at p. 5.) Second, Ortho-McNeil notes that the word "pharmaceutical" is defined as "relating to the preparation, use, or sale of medicinal drugs," The Oxford English Dictionary, at p. 662 (2d ed., Vol. XI, 1989)), and that "composition" is defined as "[t]he forming (of anything) by combination of various elements, parts, or ingredients," id., vol. III, p. 624. Accordingly, it argues, a "pharmaceutical composition" should be understood as a medicinal drug formed by combining two or more active ingredients.

In response, Kali points out that Dr. Raffa, a co-inventor of the '691 patent, stated in his deposition testimony that he "would not expect it to make a difference" whether tramadol and acetaminophen were administered mixed

together or separately to test mice, "as long as they were given within a reasonable proximity in terms of time." (Brown Decl., Ex. 16, p. 301, ll. 6-12.) While this testimony may indicate that the two methods of administration are equally effective, Dr. Raffa was not purporting to construe "pharmaceutical composition" in his testimony. He was only asked whether the method used to administer the two drugs would affect the test results in the specification. Furthermore, although Dr. Raffa could not recall which method of administration was used during the mice testing (Brown Decl., Ex. 16, p. 300, ll. 16-21), the specification indicates that the mice were indeed given "combined doses of tramadol hydrochloride and acetaminophen." '691 patent, col. 8, ll. 16-17.

Kali also cites for support the Federal Circuit's decision in PIN/NIP, Inc. v. Platte Chem. Co., 304 F.3d 1235, 1245 (Fed Cir. 2002), where the Court construed the claim limitation, "composition," to mean "a mixture that is formed at any time during use, such as through simultaneous application of the constituent chemicals, as long as a mixture is indeed formed." PIN/NIP, however, did not involve pharmaceuticals, or the limitation "pharmaceutical composition," and in any event, there is nothing in the intrinsic evidence that supports Kali's proposed claim construction, and much that supports Ortho-McNeil's.

In sum, after examining the intrinsic and extrinsic evidence, the Court

construes "pharmaceutical composition" to mean a medicinal preparation comprising an intimate admixture, prepared outside the body, generally in the form of a dosage unit, such as a tablet or capsule.

**B. Infringement**

The Court must engage in two inquiries to determine whether Kali and Teva/Barr have infringed Claim 6 of the '691 patent. First, as the Court has already done, the meaning and scope of the claim being asserted as infringed must be construed as a matter of law. See Bayer AG, 212 F.3d at 1247; Markman, 52 F.3d at 976. Second, the construed claim is then compared to the product accused of infringement. Markman, 52 F.3d at 976. Determining whether the accused device infringes the construed claim is a question of fact. See SRI Int'l v. Matsushita Elec. Corp. of Am., 775 F.2d 1107, 1125 (Fed Cir. 1985). The patentee bears the burden of proving "by a preponderance of the evidence that the accused device infringes one or more claims of the patent either literally or under the doctrine of equivalents." Advanced Cardiovascular Sys. Inc. v. Scimed Life Sys. Inc., 261 F.3d 1329, 1336 (Fed Cir. 2001). In this case, Ortho-McNeil accuses Defendants of infringing Claim 6 both literally and under the doctrine of equivalents. Defendants seek summary judgment of non-infringement; Ortho-McNeil argues that genuine issues of material fact exist, precluding summary

judgment.

**1. Literal Infringement**

To prove literal infringement, the patentee must show "that the accused device contains each limitation of the asserted claim(s)." Bayer AG, 212 F.3d at 1247 (citing Mas-Hamilton Group v. LaGard, Inc., 156 F.3d 1206, 1211 (Fed. Cir. 1998)). "If any claim limitation is absent from the accused device, there is no literal infringement as a matter of law." Id.

Typically, the "accused device" is one that is already being manufactured, marketed, or sold when an infringement suit is brought, but in the Hatch-Waxman Act context this is not the case. Under 35 U.S.C. § 271(e)(2)(A) the submission of an ANDA, with the purpose of obtaining the FDA's approval to manufacture, use, or sell a drug claimed in a patent, is defined as "an act of infringement." It is only an act of infringement, however, in the sense that it "creates case-or-controversy jurisdiction to enable the resolution of an infringement dispute before the ANDA applicant has actually made or marketed the proposed product." Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348, 1365 (Fed. Cir. 2003). This "artificial" act of infringement is not determinative of whether Defendants are liable for infringement; instead the issue "is determined by traditional patent infringement analysis, just the same as it is in other infringement suits . . . the only difference

being that the inquiries now are hypothetical because the allegedly infringing product has not yet been marketed." Id. Therefore, the Court must determine "[w]hat is likely to be sold, or, preferably, what will be sold, [in order to] ultimately determine whether infringement exists."[18] Glaxo, Inc. v. , Ltd., 110 F3d 1562, 1570 (Fed Cir. 1997).

**a. Teva/Barr's Literal Infringement Summary Judgment Motion**

Teva/Barr have stipulated that should Barr's ANDA be approved, Barr is "likely to sell the products defined in that ANDA, including tablets within the full range of the content uniformity standards specified in the ANDA." (Pritikin Decl., Ex. 2, at 2.) The content uniformity standards in Barr's ANDA permit Barr to produce a tablet with a tramadol to acetaminophen weight ratio as low as 1:6.41.[19] In light of this stipulation, counsel for Teva/Barr conceded on the record at oral

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[18] As mentioned above, on April 22, 2005 and July 26, 2006, Kali and Barr, respectively, commenced selling their generic products after their ANDAs received FDA approval. Because no party has made a motion relating to the product Defendants are in fact selling today, the Court's analysis is restricted to Ortho-McNeil's Hatch-Waxman Act infringement claim under 35 U.S.C. § 271(e)(2)(A).

[19] See Stanski Inf. Rep., Ex. 12, at TLTD006201, TLTD006397; OMP Facts, at ¶¶ 44-47 (Teva's ANDA states that the "content uniformity" of its tablets may vary according to the U.S. Pharmacopoeia standards as approved by the FDA; those standards permit variations of +/- 15 percent for each active ingredient).

argument that "should the Court construe 'about 1:5' to cover 1:6.4[1] or greater, there would be no triable issue of fact [on infringement] as to Teva." (Oral Arg. Tr. of July 21, 2006, at p. 89:9-15, 21-25.) Because the Court has indeed construed "about 1:5" to encompass ratios greater than 1:6.41, not only will Teva/Barr's motion for summary judgment of non-infringement be denied, but the Court will grant summary judgment of infringement for Ortho-McNeil against Teva/Barr. Although Ortho-McNeil did not cross-move for summary judgment, the Court "already is engaged in determining whether a genuine issue of material fact exists and the parties have been given an opportunity to present evidence designed either to support or refute the request for the entry of judgment," and thus, "[t]he grant of judgment for the nonmoving party clearly is proper [since here] both sides agree that there are no material fact issues and join in the request that the case be decided . . . ." 10A Wright, Miller & Kane, Federal Practice and Procedure (Civil) § 2720 at 346 (3d ed. 1998); see also id. at 347 ("The weight of authority . . . is that summary judgment may be rendered in favor of the opposing party even though the opponent has made no formal cross-motion under Rule 56.").

**b. Kali's Literal Infringement Summary Judgment Motion**

### i. The Role of the ANDA in Determining Literal Infringement

Unlike Teva/Barr, Kali has not stipulated that it is likely to sell a generic Ultracet with a weight ratio at or below 1:7.1. Focusing on Kali's ANDA specification, Ortho-McNeil argues that Kali is likely to sell a drug that infringes Claim 6.

A pharmaceutical manufacturer like Kali must submit an ANDA to the FDA to receive expedited approval of a generic version of a drug the FDA has previously approved. See Bayer AG, 212 F.3d at 1244 (citing 21 U.S.C. § 355(j)). An ANDA contains a specification, which describes the applicant's product. This description limits what the applicant is legally permitted to sell once the ANDA is approved. Id. at 1248-50. Selling a drug outside of the ANDA's parameters exposes the generic manufacturer to various civil and criminal penalties. Id. at 1249-50.

Kali's ANDA states that it intends to sell a drug identical to Ultracet, containing 37.5 mg of tramadol and 325 mg of acetaminophen, and possessing a weight ratio of 1:8.67. However, like Barr's ANDA, Kali's ANDA specification permits the actual weight of each active ingredient to vary either higher or lower

by 15 percent.[20] Ortho-McNeil points out that this 15 percent variation would lawfully permit Kali to sell a tablet containing as much as 43.125 mg of tramadol and as little as 276.25 mg of acetaminophen. Such a tablet would have a weight ratio of 1:6.41, and therefore, would literally infringe the 1:3.6 to 1:7.1 scope of the "about 1:5" limitation. Thus, because the ANDA permits Kali to legally sell a product that infringes Claim 6, Ortho-McNeil argues that literal infringement has been conclusively established, and that the Court *may not* examine additional evidence.

Kali concedes that the ANDA would permit it to sell an infringing product, but argues that this is not conclusive of whether it is likely to do so. Kali argues that the Court may look beyond the ANDA and examine any other relevant evidence, including the results of tests conducted on samples of the drug it proposes to sell, called a "biobatch," submitted to the FDA in order to demonstrate that its generic drug will indeed be the "bioequivalent" of Ultracet. See Bayer AG, 212 F.3d at 1249 (citing 21 U.S.C. § 355(j)(2)(A); 21 C.F.R. § 314.94(a)(7)). Kali claims that the content uniformity tests performed on its biobatch samples demonstrate that the actual pills they are likely to sell do not literally infringe

[20] See Kushan Decl., Ex. 6 at KAL 003228; OMP Facts, at ¶¶ 41-49 (Kali's ANDA explicitly permits a +/- 15 percent variation in the active ingredients).

"about 1:5."

The Court agrees with Kali that, in this particular case, the parameters of the ANDA specification are not determinative of whether Kali is likely to sell a literally infringing product, and therefore, the Court may examine additional evidence, including the biobatch test results. The Federal Circuit has explained that the plain language of 35 U.S.C. § 271(e)(2) does not "mandate an infringement analysis limited to the scope of the approval sought [in the ANDA]," and therefore, the infringement "inquiry must be based on *all of the relevant evidence*, including the ANDA." Glaxo, 110 F.3d at 1567-68 (emphasis added). In certain situations (although this is not one of them), there is no need for a district court to examine relevant evidence outside of the ANDA. This occurs when either: (A) the entire scope of the compound described in the ANDA falls *outside* the scope of the plaintiff's asserted patent, and thus, legally, the defendant *cannot infringe* the patent; or (B) the entire scope of the compound described in the ANDA falls *inside* the scope of the plaintiff's asserted patent, and thus, legally, the defendant *cannot avoid infringing* the patent. In either situation A or B, the "'well-defined compound'" that the Defendant seeks approval to sell will either certainly infringe or certainly not infringe, *regardless of where the actual product eventually sold falls within the boundaries of the ANDA specification's*

*description*. In such a case, "'the ultimate question of infringement is usually straightforward,'" see Bayer AG, 212 F.3d at 1250 (quoting Glaxo, 110 F.3d at 156)), and so, there is no reason to go outside the ANDA because "the ANDA directly addresses the question of infringement."[21] Id.

An example of situation A was presented in Bayer AG v. Elan Pharm. Research Corp., 212 F.3d 1241 (Fed Cir. 2000). In that case, the plaintiff's patent claimed a compound called nifedipine, with an SSA[22] of 1 to 4 square meters per gram ("m2/g"). The defendant generic manufacturer filed an ANDA that would permit it to sell nifedipine with an SSA of 5 m2/g or greater. Because the SSAs of these two compounds are exclusive of each other, the Federal Circuit stressed that "the only drug [the defendant generic manufacturer] can produce upon approval of

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[21] The Federal Circuit has suggested in dicta that even in cases where an ANDA's description falls wholly within or without the scope of the asserted claim, there is still no *prohibition* on a district court examining evidence outside of the ANDA (as argued by Ortho-McNeil), since it is possible, "at least in theory, that other evidence may directly contradict the clear representations of the ANDA and create a dispute of material fact regarding the identity of the compound that is likely to be sold following FDA approval." Abbott Labs. v. TorPharm, Inc., 300 F.3d 1367, 1373 (Fed. Cir. 2002). Thus, even if the instant case were one where the ANDA's description made it legally certain or legally impossible for Defendants to infringe Claim 6, the Court could likely still examine the biobatch lab results and other relevant evidence outside the ANDA.

[22] SSA is the total surface area of a solid particle divided by the particle's weight. Bayer AG, 212 F.3d at 1245 n.3.

the ANDA at issue is a drug that does not literally infringe the [plaintiff's] patent." Id. at 1250. Thus, the Court found that the defendant's "ANDA *mandates* a finding of no literal infringement" and declined to look to the defendant's biobatch test results. Id. at 1249 (emphasis added).[23] Similarly, in Caraco, because the generic manufacturer's ANDA, unlike Defendants' ANDAs here, legally prevented it from making an Ultracet generic with a weight ratio less than 1:7.5, the Federal Circuit held that "there can be no literal infringement," simply on the basis of the ANDA. 2007 U.S. LEXIS 1133, at *19.

Conversely, one could imagine an example of situation B. If in Bayer AG, the defendant's ANDA indicated that it sought approval to sell nifedipine with an SSA of *2 to 3* m2/g, this range would fall completely within the 1 to 4 m2/g range of the asserted claim. As a result, the only drug the defendant would have been able to produce upon approval of the ANDA would have been a drug that literally

[23] Warner-Lambert Co. v. Apotex Corp., 316 F.3d 1348 (Fed Cir. 2003) is another example of situation A. There, the Federal Circuit again explained that in a Hatch-Waxman Act case, "[t]he infringement [determination] is . . . limited to an analysis of whether what the generic drug maker is requesting authorization for in the ANDA would be an act of infringement if performed." Id. at 1364. In Warner-Lambert, just as in Bayer AG, the answer was "no," since "the request to make and sell a drug labeled with a permissible (non-infringing) use cannot reasonably be interpreted as an act of infringement (induced or otherwise) with respect to a patent on an unapproved use . . . ." Id. at 1364-65. Accordingly, the ANDA definitively resolved the infringement issue, and there was no need to look beyond it.

infringed the plaintiff's patent, and accordingly the ANDA itself would mandate a finding of literal infringement. See Abbott Labs. v. TorPharm, Inc., 300 F.3d 1367, 1373 (Fed. Cir. 2002) ("If an ANDA specification defines a property of a compound such that it *must* meet a limitation of an asserted claim, then there will almost never be a genuine dispute of material fact that the claim is infringed with respect to that limitation." (emphasis added)).

Not every case is so clear-cut. Often, the ANDA is not conclusive of whether what is likely to be sold will or will not infringe, because the ANDA specification's description of the product is broad enough to permit the applicant to sell both a product that infringes and a product that does not infringe. In this category of cases, "the ANDA specification . . . d[oes] not define the compound in a manner that directly addresse[s] the issue of infringement." Bayer AG, 212 F.3d at 1250. For example, in Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 1565-66 (Fed. Cir. 1997), the plaintiff's patent claimed products containing a compound called "Form 2" ranitidine hydrochloride ("RHCl"). Id. at 1565-66. The defendant's ANDA sought permission to sell a product containing at least 90% "Form 1" RHCl. The scope of the ANDA's description was broad enough to permit the Form 1 RHCl to contain impurities that could contain Form 2 RHCl. Id. at 1564, 1567. The plaintiff argued, similarly to Ortho-McNeil here, that it was

error to focus "on what [the defendant] will sell under the ANDA if and when the ANDA is approved, instead of focusing solely on the fact that the scope of approval sought by [the defendant] would allow it to manufacture compositions containing Form 2 RHCl." Id. at 1567. The Federal Circuit rejected that argument, stating that, "especially in a case such as this, involving a compound capable of existing in various forms" (i.e., an infringing form, and a non-infringing form), the "inquiry must be based on all of the relevant evidence, including the ANDA." Id. at 1568.

Another example of a case falling into this category came before this Court in 2005 in In re Gabapentin, 393 F. Supp. 2d 278, 287 (D.N.J. 2005). There, the plaintiff's patent claimed a compound containing "less than 20 ppm[24]" chloride. Id. at 281-82. The defendant's ANDA sought to market the same compound with a level of chloride "anywhere from 0 ppm to 100 ppm," a range that "includes the infringing range of less than 20 ppm chloride." Id. at 287. The plaintiffs there, as Ortho-McNeil does here, urged the Court to "assume that Defendants will sell [the compound] with the lowest possible chloride permitted by their ANDA and, in doing so, will infringe the [asserted] patent." Id. However, because the ANDA did "not address the precise infringement issue before the Court," the Court

[24] "ppm" is short for "parts per million."

declined to confine its analysis to the ANDA, and "look[ed] to all the relevant evidence, including biobatch data results and additional testing of [the defendant's ANDA product]." Id.

The Court will do the same here, as the case before it is clearly not one in which the scope of the ANDA's specification legally requires Defendant to sell an infringing product. Claim 6 has been construed to encompass weight ratios ranging from 1:3.6 to 1:7.1. Kali's ANDA permits it to sell a product with a weight ratio as low as 1:6.41, which would infringe Claim 6, but also a product with a weight ratio above 1:7.1, which would not infringe. Thus, the ANDA does not directly resolve the precise infringement issue, and the Court will examine additional evidence.

**ii. The Biobatch Test Results**

During discovery, Kali produced actual samples of its tramadol/acetaminophen tablets, and the results from tests it performed on five batches of its product it submitted to the FDA as a part of the ANDA approval process. The five batches were made in the same manner as Kali's commercial product was to be made, as described in its ANDA. Kali tested 170 tablets randomly sampled from the five batches, and recorded how many milligrams of tramadol and acetaminophen each tablet contained, by what percentage that

amount deviated from Kali's target of 37.5 mg of tramadol and 325 mg of acetaminophen, and the resulting tramadol/acetaminophen weight ratio. The results demonstrate that Kali is able to consistently produce a tablet with a weight ratio very close to 1:8.67. The closest any one tested tablet came to a weight ratio of 1:7.1, the high end of the "about 1:5" infringement range, is a relatively distant 1:8.26. (Subramanian Decl., Ex. 1; Stanski Inf. Rep., Ex. 12, at KAL019195, KAL019245.)

Ortho-McNeil points out that one particular tested tablet contained 11.6 percent less tramadol than the target 37.5 mg (Subramanian Decl., Ex. 1 (Batch EB 090, Content Uniformity - Middle, Tablet 6).), and hypothesizes that a tablet having a similar 12 percent variance in each of its two active ingredients could possess a weight ratio as low as 1:6.81, which dips into the infringement range.[25] Given this possibility, Ortho-McNeil argues that a genuine material fact question exists, and summary judgment is inappropriate.

The Court disagrees. While the hypothetical tablet above would indeed infringe, Ortho-McNeil has presented no evidence showing that Kali is *likely* to make such a tablet. The tablet that tested for 11.6 percent less tramadol had an

[25] This hypothetical infringing tablet would have 12 percent less acetaminophen (286 mg), and 12 percent more tramadol (42 mg).

overall weight ratio of 1:9.72 (id.), which is well outside the infringement range. No other tablet tested had even a 10 percent variance, either higher or lower, from its target amounts of each active ingredient. (Id.) Given this high degree of accuracy, no reasonable juror could conclude from the test results that Kali is likely to sell a literally infringing tablet.

Ortho-McNeil stresses that Kali could have, but chose not to, reduce the permissible 15 percent active ingredient variances that it sought in its ANDA in order to avoid infringement.[26] While true, Kali's failure to narrow this permissible variance only suggests that it sought to insulate itself from the criminal and civil penalties that might result from selling a product exceeding that permissible variance, not that it is likely to sell an infringing tablet. Indeed, it is undisputed that Kali intends to sell a tablet with a weight ratio of 1:8.67, and the test results do not show that it is likely to sell a tablet with a weight ratio of 1:7.1 or lower.

Finally, Ortho-McNeil attempts to discredit the test results by arguing that there is no evidence that the results from only 170 tablets accurately represent the characteristics of the hundreds of thousands of tablets Kali will probably sell.

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[26] Ortho-McNeil points out that the defendant in Caraco voluntarily amended its ANDA to narrow its permissible manufacturing variability to result in a range with a low point of 1:7.5 in order to avoid "about 1:5." See Caraco, 2005 U.S. Dist. LEXIS 24998, at *2-3.

However, if Ortho-McNeil is correct, then not only does its argument cast doubt on the legitimacy of the high degree of accuracy found in the test results (as it argues), but it also casts doubt on the legitimacy of the 11.6 percent variance found in the one tablet that Ortho-McNeil relies so strongly on. Without that isolated variance, Ortho-McNeil has no evidence outside of the ANDA to suggest that Kali will sell an infringing tablet. In any event, the Federal Circuit has said that "access to actual samples and the extensive technical data required by the FDA [during the ANDA process] generally removes much of the uncertainty from a court's otherwise hypothetical inquiry" into whether an ANDA applicant is likely to sell an infringing product. See Glaxo, 110 F.3d at 1569 n.2. The Court agrees with Kali that if Ortho-McNeil was not satisfied that Kali's 170 test results accurately demonstrated the nature of the product it was likely to sell, it "could have further informed the court's infringement analysis by offering analyses of these samples . . . , but it chose not to do so." Id.

Thus, the Court concludes that the undisputed material facts show that no reasonable juror could find that Kali is likely to sell a tramadol/acetaminophen tablet with a weight ratio of 1:7.1 or lower, and accordingly, Kali's motion for summary judgment as to literal non-infringement will be granted.

**2. Doctrine of Equivalents**

If Kali has not literally infringed, Ortho-McNeil argues, it has still infringed Claim 6 under the doctrine of equivalents. The doctrine of equivalents "'allows the patentee to claim those insubstantial alterations that were not captured in drafting the original patent claim but which could be created through trivial changes.'" Honeywell Int'l Inc. v. Hamilton Sundstrand Corp., 370 F.3d 1131, 1139 (Fed. Cir. 2004) (quoting Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 533 U.S. 722, 733 (2002)). Thus, if Kali's ANDA product has only insubstantial differences from Claim 6 of the '691 patent, as Ortho-McNeil asserts, then the two are equivalents, and Kali has infringed. See id.

Kali moves for summary judgment on Ortho-McNeil's doctrine of equivalents argument, relying on prosecution history estoppel, which "bar[s] a patentee from asserting equivalents if the scope of the claims has been narrowed by amendment during prosecution." Id. (citing Festo, 535 U.S. at 733-34). Kali points out that in its reissue application for the '691 patent, Ortho-McNeil cancelled, among others, Claim 1, which spanned from "about 1:1 to about 1:1600," in order to avoid anticipation by the prior art Flick patent. (See Kushan Decl., Ex. 8, at POMP00010315.) As a result, Kali argues, Ortho-McNeil surrendered all weight ratios between "about 1:5" (i.e., 1:7.1), and "about 1:1600."

The Court need not decide whether Kali's prosecution history estoppel

argument is correct. Following Ortho-McNeil v. Caraco, summary judgment of non-infringement under the doctrine of equivalents will be granted in Kali's favor pursuant to the claim vitiation doctrine. The doctrine of equivalents has no application where "a court determines that a finding of infringement under the doctrine of equivalents would entirely vitiate a particular claimed element." Freedman Seating Co. v. Am. Seating Co., 420 F.3d 1350, 1358 (Fed Cir. 2005) (quoting Lockheed Martin Corp. v. Space Sys./Loral, Inc., 324 F.3d 1308, 1321 (Fed. Cir. 2003)). In Caraco, the Federal Circuit held that Ortho-McNeil, "having so distinctly claimed the 'about 1:5' ratio, . . . cannot now argue that the parameter is broad enough to encompass, through the doctrine of equivalents, ratios outside of the [95 percent] confidence intervals expressly identified in the patent. . . . [T]o do so would eviscerate the limitation." 2007 U.S. App. LEXIS 1133, at *20. Just as in Caraco, the weight ratio of the tablet Kali intends to make in this case, 1:8.67, and the lowest weight ratio of any tablet tested in the five biobatches, 1:8.26, are beyond the 1:3.6 to 1:7.1 outer boundaries of "about 1:5" set by the confidence intervals in the '691 patent. Thus, as a matter of law, the doctrine of equivalents is unavailable to Ortho-McNeil.

To summarize, the Court will grant summary judgment of non-infringement, to Kali, both under literal infringement and the doctrine of equivalents. The Court

will deny summary judgment to Teva as to non-infringement, and will grant summary judgment to Ortho-McNeil against Teva as to literal infringement.

### C. Validity

Kali and Teva/Barr assert the invalidity of Claim 6 of the '691 patent both as defenses to infringement and in counterclaims. Kali asserts invalidity on the grounds of indefiniteness, anticipation, obviousness, and the public-use bar.[27] Teva/Barr only assert invalidity on the grounds of anticipation.

"A patent shall be presumed valid." 35 U.S.C. § 282. The party challenging the patent bears the burden of proving by clear and convincing evidence the invalidity of the claims of a patent. Id. "The 'clear and convincing' standard of proof of facts is an intermediate standard which lies somewhere between 'beyond a reasonable doubt' and a 'preponderance of the evidence'" and "has been described as evidence which produces in the mind of the trier of fact an abiding conviction that the truth of [the] factual contentions [is] 'highly probable.'" Buildex, Inc. v. Kason Indus., Inc., 849 F.2d 1461, 1463 (Fed. Cir. 1988) (internal quotation omitted).

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[27] Although the Court has granted Kali summary judgment of non-infringement, it still has jurisdiction to decide Kali's invalidity counterclaims. See Cardinal Chem. Co. v. Morton Int'l Inc., 508 U.S. 83, 95-96 (1993); Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 1540-41 (Fed. Cir. 1983).

### 1. Indefiniteness

Under 35 U.S.C. § 112, a patent "specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." This requirement is satisfied if "one skilled in the art would understand the bounds of the claim when read in light of the specification." Exxon Research & Eng'g Co. v. United States, 265 F3d 1371, 1375 (Fed Cir. 2001) (quoting Miles Labs., Inc. v. Shandon, Inc., 997 F.2d 870, 875 (Fed Cir. 1993)). Whether a patent claim is invalid for indefiniteness is a question of law. Id. at 1376.

Citing Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1217 (Fed. Cir. 1991), Kali argues that using the term "about" to increase a range renders a claim indefinite if the intrinsic evidence does not indicate what that range covers, and that here, an interpretation of "about 1:5" that encompasses 1:8.67 would therefore cause Claim 6 to fail for indefiniteness. As explained above, the Court has not interpreted "about 1:5" to extend to 1:8.67. Kali does not argue that "about 1:5" would be invalid for indefiniteness if interpreted to include a range of ratios more narrow than 1:8.67. Accordingly, Kali's motion for summary judgment of invalidity for indefiniteness will be denied.

### 2. Anticipation

Under 35 U.S.C. § 102(b), a person is not entitled to a patent if the alleged invention was "described in a printed publication . . . more than one year prior to the date of the application." This standard is satisfied if two requirements are met. First, there must be "identity of the invention," or in other words, "each and every element as set forth in the claim [must be] found, either expressly or inherently described, in a single prior art reference." Constant v. Advanced Micro-Devices Inc., 848 F.2d 1560, 1570 (Fed. Cir. 1988). Second, the prior art reference must enable the person of skill in the art to make the invention. In Re Sasse, 629 F.2d 675, 681 (C.C.P.A. 1980). "[P]rior art references are presumed to be enabling." Id. Anticipation is a question of fact. In re McDaniel, 293 F.3d 1379, 1382 (Fed. Cir. 2002).

Ortho-McNeil filed its application for the '691 patent on September 6, 1991. Thus, the critical date for the '691 patent is one year earlier, September 6, 1990. Kali and Teva/Barr assert that Claim 6 is anticipated by the Flick patent. Kali alone asserts that Claim 6 is also anticipated by a prior art article called "the Sorge reference."

**a. The Flick Patent**

The Flick patent issued on March 28, 1972. It discloses tramadol and related compounds, and the processes for making these compounds. '589 patent,

cols. 1-5. In addition, the patent specification states in example 22 that tramadol has "proven to be of considerable therapeutic value when used in combination with other therapeutically active agents" such as "other analgesics" (the "use-in-combination teaching"). '589 patent, col. 12, ll. 45-50. After listing several classes of drugs in addition to analgesics that could be effectively combined with tramadol, the specification states: "The following example illustrates the composition of such combination preparations without, however, limiting the same thereto." '589 patent, col. 12, ll. 62-64. Example 23 then follows, and it discloses a tablet containing 25 mg of tramadol, 250 mg of "p-acetamino phenol," which the parties agree is another term for acetaminophen,[28] and two other compounds.[29] '589 patent, col. 12, ll. 66-75.

There is no dispute that example 23 discloses the first two limitations of Claim 6: (1) a "pharmaceutical composition," (2) "comprising a tramadol material

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[28] Some of Ortho-McNeil's briefing suggests that it disputes whether "p-acetamino phenol" is a synonym for acetaminophen. However, counsel for Ortho-McNeil conceded on the record during oral argument that, while it is a "very, very, obscure term," it indeed is synonymous with acetaminophen. (Oral Arg. Tr. of July 21, 2006, at 125:9-17.)

[29] Those two other compounds are pentobarbital sodium (a sleep-inducing barbiturate, at 30 mg), and ethoxy benzamide (an analgesic, at 250 mg). (OMP Facts ¶ 55.)

and acetaminophen."[30] However, because example 23 only discloses tramadol and acetaminophen in a 1:10 weight ratio (25 mg of tramadol, and 250 mg of acetaminophen), Ortho-McNeil argues that the Flick patent fails to disclose the "about 1:5" limitation of Claim 6, and therefore does not anticipate the '691 patent.[31]

Kali and Teva/Barr claim that example 23 discloses "about 1:5" when read in conjunction with the rest of the specification. After a series of examples describing how to make different compositions containing tramadol, such as tablets, solutions, capsules, and suppositories, example 22 instructs that "[o]f course, by variation and calculation of the ingredients tablets and other compositions are prepared containing lower or higher amounts of the essential

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[30] See Pl.'s Supp. Br. at p. 11; OMP Facts ¶ 55. Even though the tablet in example 23 contains two active ingredients in addition to tramadol and acetaminophen, the tablet still meets the "comprising a tramadol material and acetaminophen" limitation of Claim 6, because the patent law term of art "comprising" denotes a set of listed ingredients that is fully open to the inclusion of additional ingredients. See, e.g., PPG Indus. v. Guardian Indus. Corp., 156 F.3d 1351, 1354 (Fed. Cir. 1998) (citing Manual of Patent Examining Procedure § 2111.03 (6th ed. 1997)). In contrast, if the '691 patent authors intended for Claim 6 to always contain *only* tramadol and acetaminophen, they could have used the term of art, "consisting of," in order to exclude additional ingredients. See id.

[31] Ortho-McNeil does not argue that if identity does exist between the Flick patent and the '691 patent, that Flick does not enable the person of ordinary skill to make the compound. Thus, identity is the only issue before the Court with regard to Flick and anticipation.

active agents as desired" (the "vary-as-desired teaching"). '589 patent, col. 11, ll. 54-57. A few paragraphs later, example 22 also instructs that "[o]ral administration of single doses between about 25 mg. and about 100 mg. *and preferably of 50 mg.* or 75 mg. . . . proved to be highly effective" in testing. '589 patent, col. 12, ll. 24-31 (emphasis added). Defendants argue that therefore, the Flick patent teaches that it is permissible to increase the 25 mg tramadol dose in example 23 to the 50 mg preferred oral dose in example 22. When 50 mg of tramadol is combined with the 250 mg of acetaminophen disclosed in example 23, the resulting compound has a weight ratio of exactly 1:5, and thus, argue Defendants, anticipates Claim 6.

In response, Ortho-McNeil asserts that the vary-as-desired, and 50 mg teachings are not applicable to the composition in example 23, because the teachings are found in a part of the specification that addresses tramadol-only compositions. It argues that this section is separate from, and unrelated to, the portion of the specification discussing compositions containing tramadol and other active ingredients, such as that in example 23.

The Court agrees with Defendants, and finds that the Flick patent expressly discloses the "about 1:5" limitation. Although the vary-as-desired and 50 mg teachings do appear in a portion of the specification that has yet to describe

compositions other than those containing only tramadol, there is nothing in the specification to suggest that the relative placement of those teachings means that tramadol can no longer be varied as desired, or is no longer preferable and highly effective at 50 mg when included in a composition containing another active ingredient. In other words, the teachings of example 22 describe features of the tramadol compound itself. The specification does not say that these features are dependent upon tramadol being the only active ingredient in a particular composition. In fact, the language used by the inventors and the structure of the specification suggest that the vary-as-desired and 50 mg teachings are relevant to the patent's teaching that tramadol can be used in combination with other analgesics, including acetaminophen.

First, the language of the vary-as-desired and 50 mg teachings indicate that they have broad application. The vary-as-desired teaching states very generally that "*tablets and other compositions*" may contain higher or lower amounts of tramadol as desired--not tablets and compositions containing only tramadol. See '589 patent, col. 11, l. 55 (emphasis added). Similarly, the 50 mg teaching is presented as applying generally to "[o]ral administration of single doses." '589 patent, col. 12, l. 24. Example 23 clearly describes a composition in the form of an orally administered tablet. If the vary-as-desired teaching's "tablet" does not

include example 23's "tablet," surely the inventors would have explicitly said so. They did not.

Second, the proximity of the vary-as-desired and 50 mg teachings to the specification's use-in-combination teaching indicates that these teachings are very much relevant to each other. Indeed, all three teachings appear in the same example, number 22, as opposed to being located in remote sections of the specification. In fact, the use-in-combination teaching appears only three paragraphs after the 50 mg teaching. Example 23 follows immediately thereafter.

Third, the use-in-combination teaching states that it applies to "[t]he compounds according to the present invention." '589 patent, col. 12, l. 45. "[C]ompounds," of course includes tramadol, and "according to the present invention" (as explained by the specification), tramadol's dosage can be increased to a 50 mg dosage. There is no indication that the phrase "compounds according to the present invention" incorporates tramadol only if devoid of its previously-described features.

Fourth, immediately after the use-in-combination teaching, example 22 states that example 23 is intended to "illustrate the composition of such combination preparations *without, however, limiting the same thereto*." (emphasis added). With these words, the inventors further indicated that the exact

parameters of example 23's tablet are not etched in stone, and can be varied according to the teachings of the specification.

Fifth, and finally, example 23 itself makes clear that it must be read in conjunction with the rest of the specification. Immediately after example 23 discloses the tramadol/acetaminophen tablet, the specification states that, "[o]f course, *many changes and variations in the starting materials* and reaction components, . . . may be made by those skilled in the art *in accordance with the principles set forth herein* . . . ." '589 patent, col. 13, ll. 1-7 (emphases added). On its face, this paragraph appears to permit the "starting materials," including the 25 mg of tramadol to be adjusted, and incorporates the "principles set forth herein," such as the vary-as-desired and 50 mg teachings, as guidance for how to do so. Read as a whole, the Flick patent expressly anticipates a pharmaceutical composition comprising 50 mg of tramadol and 250 mg of acetaminophen in a weight ratio of 1:5.

The Federal Circuit addressed a similar situation in Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc., 246 F.3d 1368, 1372, 1378 (Fed. Cir. 2001). In that case, the Court of Appeals affirmed summary judgment of anticipation where the invalidated patent claimed a method for treating cancer patients by (1) administering 135 to 175 mg/m2 of the compound traxol, and (2) premedicating

the patient with an unspecified drug to treat hypersensitivity reactions to the traxol. Id. at 1372. The anticipating prior art reference (the "Kris reference") disclosed treatment of cancer patients with traxol in amounts both within and above the claimed 135 to 175 mg/m2 range. The Kris reference also observed that patients treated with 190 mg/m2 of traxol and above experienced hypersensitivity reactions, and therefore suggested that "[f]urther studies are needed to see if pretreatment regimens, . . . will permit the safe administration of this compound." Id. The Court rejected the patent holder's argument that because only patients receiving 190 mg/m2 of traxol and above suffered hypersensitivity reactions, Kris did not disclose pretreating patients receiving traxol in the claimed dosage range. The Court explained that despite the fact that "Kris's suggestion of premedication is primarily directed to patients receiving higher doses [of traxol] who experienced hypersensitivity reactions," the reference anticipated the patent because "Kris did not confine his pretreatment suggestion only to patients given higher doses." Id. at 1379. Similarly here, despite the fact that Flick's vary-as-desired and 50 mg teachings may seem to be primarily directed towards tramadol-only compositions, Flick did not confine these teachings to such compositions, as explained in detail above.

The Court's conclusion is also consistent with Ecolochem, Inc. v. Southern

California Edison Co., 227 F.3d 1361 (Fed. Cir. 2000), which Ortho-McNeil cites for support. In Ecolochem, the Federal Circuit reversed a finding of anticipation as to a patent that claimed a process requiring a step of passing a liquid containing oxygen and hydazine through activated carbon. Id. at 1365. The prior art contained a figure ("Figure 10") disclosing a similar process where an analogous step passed water containing oxygen and *hydrogen* through activated carbon. Id. The Federal Circuit explained that it would not impute the use of hydrazine in a separate, unrelated section of the prior art reference into Figure 10 in order to anticipate the patent, because the authors of the prior art reference, "very carefully made sure," using headings and language, "that Figure 10 refers only to hydrogen and not to hydrazine." Id. at 1369. As explained above, the specification of the Flick patent does not "very carefully make sure" that the vary-as-desired and 50 mg teachings described tramadol only when used in a single-agent composition.

Ortho-McNeil attempts to create a genuine issue of material fact for trial by submitting the invalidity expert report of Dr. Stanski, who opines that "the Flick patent would not have disclosed the four required elements of claim 6 to one of ordinary skill, particularly the requirement that the Tramadol and [acetaminophen] be present in a . . . weight ratio of about 1:5." (Stanski Val. Rep. ¶ 99.) While properly-supported expert testimony can certainly raise a genuine issue of material

fact, the mere submission of the affidavit of an expert who avers that a prior art reference is not anticipatory, in and of itself, is not sufficient to meet this evidentiary threshold. See Novartis Corp. v. Ben Venue Labs., Inc., 271 F.3d 1043, 1051 (Fed Cir. 2001). The expert "must set forth the factual foundation for his opinion . . . in sufficient detail for the court to determine whether that factual foundation would support a finding [of validity] . . . ." Id. The standard of "the factual foundation necessary to support an expert's opinion" is a matter of regional circuit law. Id.

> [T]he Third Circuit has demanded that the factual predicate of an expert's opinion must find some support in the record, and has emphasized that mere "theoretical speculations" lacking a basis in the record will not create a genuine issue of fact. Penn. Dental Ass'n v. Med. Serv. Ass'n., 745 F.2d 248, 262 (3d Cir. 1984). Moreover, where an expert's opinion is predicated on factual assumptions, those assumptions must also find some support in the record. Shaw v. Strackhouse, 920 F.2d 1135, 1142 (3d Cir. 1990).

Id.

Dr. Stanski bases his opinion on a number of factual observations. However, because the Court finds that all of these observations are either legally irrelevant, or unsupported by the record, Dr. Stanski's report fails to create a genuine issue of material fact for trial. First, Dr. Stanski states that a person of ordinary skill would reject the Flick patent's teaching that when Tramadol is combined with other active ingredients, "frequently a synergistic effect is

observed" (Stanski Val. Rep. ¶ 91), and would also reject that the specific compound disclosed in example 23 would exhibit synergism, (Stanski Val. Rep. ¶ 94.). True or not, these observations are immaterial to whether the Flick patent anticipates the '691 patent because synergy is not an element of Claim 6, or any claim in the '691 patent for that matter.[32]

Second, Dr. Stanski asserts that the section of the Flick specification containing the vary-as-desired and 50 mg teachings "says nothing at any point that could be considered guidance on selecting doses for use in combination products." (Stanski Val. Rep. ¶ 98.) He also claims that it "provides no suggestion that the dosing options for single-agent Tramadol products is to be used in multi-agent formulations." (Id.) These factual allegations are not supported by the record. As discussed above, the Flick patent says the vary-as-desired teaching is applicable to "tablets and other compositions," and that the 50 mg teaching applies to "[o]ral administration of single doses" of tramadol, with no suggestion that example 23 is

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[32] Ortho-McNeil also argues, without citation to Dr. Stanski's report, that the Flick patent teaches away from the "about 1:5" limitation because a person of skill in the art seeking to alter example 23 to achieve synergistic effects would decrease, not increase, the 25 mg of tramadol in the composition. (Pl.'s Opp'n. Br. p. 29.) However, "the question whether a reference 'teaches away' from the invention is inapplicable to an anticipation analysis." See Bristol-Myers Squibb, 246 F.3d at 1378. "A reference is no less anticipatory if, after disclosing the invention, the reference then disparages it." Celeritas Techs. v. Rockwell Int'l Corp., 150 F.3d 1354, 1361 (Fed. Cir. 1998).

somehow not also an orally administered tablet or other composition.

Third, to illustrate these assertions, Dr. Stanski states: "For example, the references throughout the section refer to a single agent, not plural agents." (Stanski Val. Rep. ¶ 98.) While it is undisputed that examples 17 through 22 illustrate compositions that contain only tramadol, Dr. Stanski overlooks that example 22's vary-as-desired teaching itself explicitly mentions "plural agents." It states that "compositions are prepared containing lower or higher amounts of the essential active *agents* as desired." '589 patent, col. 11, ll. 55-57 (emphasis added). This further suggests that this teaching applies to compounds with multiple active ingredients, and Dr. Stanski's failure to acknowledge this aspect of the record further undermines his opinion that the teaching does not apply to example 23.

Fourth, Dr. Stanski next notes "that Example 23 itself provides no suggestions that its components are or should be varied." (Stanski Val. Rep. ¶ 98.) This of course, ignores that immediately after disclosing its tramadol-acetaminophen composition, example 23 instructs that "many changes and variations in the starting materials . . . may be made by those skilled in the art in accordance with the principles set forth herein . . . ." '589 patent, col. 13, ll. 1-8. It is difficult to imagine a more explicit suggestion to vary the components of

example 23's tablet.

In light of the above, the Court concludes that Dr. Stanski's opinion that the vary-as-desired and 50 mg teachings do not apply to example 23 is not based on legally relevant facts, or on facts supported by the record. Thus, Dr. Stanski's report is insufficient to create a genuine issue of material fact for trial on the issue of anticipation.

Ortho-McNeil makes three final arguments. First, Ortho-McNeil claims that the deposition testimony of Kali's expert on pharmacology, Dr. Charles Inturrisi, creates an issue of fact as to whether the Flick patent anticipates "about 1:5." Dr. Inturrisi was asked by counsel for Ortho-McNeil: "There's no specific disclosure in [the Flick] patent containing a ratio of 1 to 5?" (Hatcher Decl., Ex. 4 at 234:16-19.) Dr. Inturrisi responded, "That's correct." (Id. l. 19.) Read in isolation, Dr. Inturrisi's admission might seem to raise an issue of fact. However, Ortho-McNeil leaves out important context that makes it apparent that Dr. Inturrisi was only testifying that there is no example in the Flick patent disclosing a tramadol-acetaminophen tablet in a weight ratio of 1:5 that is on par with the 1:10 tablet in example 23. Immediately before Dr. Inturrisi's above quoted statement he was asked, "Now the ratio of tramadol to acetaminophen in example 23 is 1 to 10, correct?" Dr. Inturrisi replied, "That's correct." Thus, counsel's use of the phrase

"specific disclosure" in the next question implies that he is asking whether there is a disclosure of a tablet with a 1:5 weight ratio like example 23's disclosure of 1:10. Defendants position is that the Flick patent anticipates "about 1:5" when example 23 is read in conjunction with the rest of the patent's specification. It is clear from the rest of Dr. Inturrisi's testimony that this is also how he read the Flick patent. In response to being asked whether "there is any specific statement in this patent of the amounts of tramadol and acetaminophen that can or should be combined" (Hatcher Decl., Ex. 4 at 238:4-7), Dr. Inturrisi responded, "I would say from reading [column 12, line 25, and column 12, line 45, and] example 23, they would suggest that one could use 25, 50, 75 or 100 milligrams of tramadol in combination with acetaminophen," (id. at 239:10-14). Thus, Dr. Inturrisi's testimony does not create a genuine issue of material fact for trial.

Ortho-McNeil's next argument is that Flick is not anticipatory because the inventors never actually made or evaluated the tablet disclosed in example 23. However, the Federal Circuit has said repeatedly that "anticipation does not require actual performance of suggestions in a disclosure. Rather, anticipation only requires that those suggestions be enabling to one of skill in the art." Bristol-Myers Squibb, 246 F.3d at 1379.

Ortho-McNeil also asserts that the "form of expression" of example 23

shows that the tablet is only "hypothetical," and "prophetic." (Pl.'s Opp'n Br. p. 26.) However, the speculative or conjectural tenor of a prior art reference is also irrelevant to anticipation. See Ciba-Geigy, 864 F. Supp. at 437. "All that matters is whether the [prior art] identifies the invention described in [the claims]." Id.

In sum, the Flick patent specifically describes a tablet containing 25 mg of tramadol material and 250 mg of acetaminophen in example 23. When changed and varied "in accordance with the principles set forth [in the patent]," including the specification's teachings to (1) use a "higher amount[]" of tramadol "as desired," and (2) use the preferred and "highly effective" oral tramadol dose of 50 mg, that tablet possesses a weight ratio of 1:5. Thus, all four limitations of Claim 6 of the '691 patent are anticipated by the Flick patent. A reasonable fact finder could not conclude otherwise. Defendants' motions for summary judgment of invalidity for anticipation will be granted.

**b. The Sorge Reference**

In addition to the Flick patent, Kali argues that a publication authored by two German doctors, Dr. Sorge and Dr. Pichlmayr ("the Sorge reference"), anticipates Claim 6 of the '691 patent. The Sorge reference discusses using orally administered analgesics to treat pain in patients with gynecologic cancerous illnesses. (Brown Decl., Ex. 17, at TR000005-10.) The article discloses using the

World Health Organization ("WHO")'s three-stage plan for administering oral analgesics. (Id. at TR000006.) In the first stage of the plan, Sorge teaches the prescription of a "peripherally acting analgesic[]," such as acetaminophen at a 500 to 1000 mg individual dosage every 4 to 6 hours.[33] (Id. at TR000006-08.) If sufficient pain relief is not achieved, the second stage involves prescribing a "weak centrally acting analgesic" (also called a "weak opioid"), such as tramadol at a 50 to 100 mg individual dosage every 4 to 6 hours. (Id.) Finally, the last step of the staged plan is to transition to a strong centrally acting analgesic (i.e., a "strong opioid"), such as morphine. (Id.)

The Sorge reference explicitly discloses combining peripherally acting analgesics with centrally acting, weak and strong opioids in this staged plan. In a section entitled "Fundamentals of Treatment with Analgesics," it states that "[i]n many cases, a combination of the centrally acting analgesics with a peripheral pain killer can be sensible . . . ." (Id.) Later on, during its discussion of "Peripheral Analgesics," Sorge states that acetaminophen "is very frequently given to patients . . . as a co-analgesic to a centrally acting pain killer." (Id. at TR000007.) In its next section, entitled "Oral Opiates in Pain Therapy," Sorge discusses the drug

[33] The Sorge reference uses term "Paracetamol" for acetaminophen. It is undisputed that these terms are synonyms.

codeine, which it states is "[t]he classical representative of the *weak opioids*," for which "[t]here is an entire series of preparations available that contain a fixed combination of codeine with a peripheral analgesic." (Id. at TR000007.) A few lines later, Sorge teaches that "[o]ther weak opioids that can be used [include] Tramadol." (Id. at TR000008.)

Despite Sorge's teachings to prescribe peripheral analgesics like acetaminophen, and weak opioids like tramadol, in combination, Kali concedes that the Sorge reference does not disclose the administration of tramadol and acetaminophen as active ingredients in a *single tablet or capsule.* (Kali Br. at 17.) Nevertheless, Kali argues that Sorge identifies all four limitations of Claim 6 because the proper construction of the phrase "pharmaceutical composition" includes the "co-administration of tramadol and acetaminophen as described in the Sorge reference." (Id.) However, the Court has construed "pharmaceutical composition" to mean a medicinal preparation comprising an intimate admixture, prepared outside the body, generally in the form of a dosage unit, such as a tablet or capsule. See supra, part III.A.2. This definition excludes the co-administration of two separate drugs, and therefore, the Sorge reference fails to identify a "pharmaceutical composition." Accordingly, the Sorge reference fails to anticipate Claim 6 of the '691 patent, and Defendants' motions for summary

judgment on this point will be denied.

### 3. Obviousness

Kali asserts that Claim 6 is invalid for obviousness. "A claimed invention is unpatentable due to obviousness if the differences between it and the prior art 'are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art.'" Akamai Techs., Inc. v. Cable & Wireless Internet Servs., Inc., 344 F.3d 1186, 1195 (Fed. Cir. 2003) (quoting 35 U.S.C. § 103(a)). Obviousness is a determination of law that is based on four underlying factual inquiries, known as the "Graham factors": (1) the level of ordinary skill in the art; (2) the scope and content of the prior art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of nonobviousness, also known as, secondary considerations. Id. (citing Graham v. John Deere Co., 383 U.S. 1, 17-18 (1966)).

Because this is a motion for summary judgment, and because a patent is presumed valid, "the accused infringer must prove by clear and convincing evidence that [the] claim that is challenged cannot reasonably be held to be non-obvious." Knoll Pharm. Co., Inc. v. Teva Pharms. USA, Inc., 367 F.3d 1381, 1383 (Fed. Cir. 2004). While Kali bears the ultimate burden of persuasion, if Kali is able to present a prima facie case of obviousness based on the first three Graham

factors, the burden of production shifts to Ortho-McNeil to demonstrate secondary considerations in order to rebut the prima facie case. See Winner Int'l Royalty Corp. v. Wang, 202 F.3d 1340, 1350 (Fed. Cir. 2000). "When rebuttal evidence is provided, the prima facie case dissolves, and the decision is made on the entirety of the evidence." In re Kumar, 418 F.3d 1361, 1366 (Fed. Cir. 2005). With these principles in mind, the Court will now examine the Graham factors.

**a. Graham Factor 1: The Level of Ordinary Skill in the Art**

The parties do not dispute the level of ordinary skill. Ortho-McNeil asserts that the person of ordinary skill in the pertinent art possesses an M.D. or Ph.D. in pharmacology, and has substantial experience regarding the administration of analgesic drugs to human patients. (Pl.'s Opp'n Br. at p. 32 n.22 (citing Stanski Val. Rep. ¶ 3).) Kali does not contest this assertion.

**b. Graham Factor 2: The Scope and Content of the Prior Art**

Although the Court has concluded in its anticipation analysis that the Flick patent anticipates Claim 6, for purposes of its obviousness analysis the Court assumes that Flick does not disclose "about 1:5," and therefore only describes a pharmaceutical composition comprised of tramadol and acetaminophen in a 1:10

weight ratio, as Ortho-McNeil argues.

In addition to the Flick patent and the Sorge reference, Kali cites six references as part of the prior art, and Ortho-McNeil does not contest their inclusion. The first reference is a 1981 article by William T. Beaver M.D., discussing "Aspirin and Acetaminophen as Constituents of Analgesic Combinations" ("the Beaver reference"). (Brown Decl., Ex. 15.) The Beaver reference demonstrates that pharmaceutical compositions containing acetaminophen and other analgesics, including weak opioids, were marketed before the '691 patent's application was filed. The Beaver reference describes products combining acetaminophen with codeine (Tylenol with Codeine®), hydrocodone (Vicodin®), oxycodone (Tylox®), and propoxyphene (Darvocet-N®). (Id. at 0200390.)

Second, Kali cites the 1986 WHO Cancer Pain Relief guidelines ("the WHO Guidelines"), which was cited by the Sorge reference. (Brown Decl., Ex. 13.) The WHO Guidelines disclose using a "three step 'analgesic ladder'" in order to treat cancer-related pain. (Id. at KAL016429.) At step one, a non-opioid such as acetaminophen is prescribed. (Id.) If the non-opioid does not provide adequate pain relief, the WHO Guidelines instruct that "codeine *or an alterative weak opioid* should be prescribed" at step two. (Id. (emphasis added).) Furthermore,

the "drug in the weak opioid group should be *added* to the [step one] medication given." (Id. at KAL016459 (emphasis added).) The WHO Guidelines explain that because non-opioids and opioids treat pain via different mechanisms, "combinations of these two types of drug produce additive analgesic effects . . . and are often used." (Id. at KAL016428.) The WHO Guidelines also advise that "[t]he dose of an analgesic should be titrated against the patient's pain, being gradually increased until the patient is comfortable." (Id. at KAL016459.)

Third, Kali cites an article entitled "Current Understanding of the Origination and Treatment of Pain," authored by Antje Beyer and Dr. K. Peter ("the Beyer reference"), which appeared in a German medical journal called "The Surgeon" in July 1990. (Brown Decl., Ex. 19.) Like Sorge, the Beyer reference discloses using the WHO Guidelines' three-step regimen for the treatment of tumor pain. (Id. at TR000056-57.) Beyer states that "[t]he first stage consists of regular administration of a so-called peripheral analgesic (Table 2)." (Id. at TR000057.) Table 2 includes "Paracetamol," i.e., acetaminophen, and discloses an oral dose every three to four hours of 500 to 1000 mg. (Id. at TR000056.) "If this is not sufficient," Beyer then states, "the next step involves the *additional* administration of a weak opiate (codeine, *tramadol*, tilidine)." (Id. at TR000057 (emphases added).) Table 3 in Beyer presents a list of weak opioid analgesics to

choose from that includes tramadol in an oral dose of 50 to 100 mg every four hours. (Id. at 000056.)

The fourth prior art reference is an August 1990 article appearing in the Swiss Journal of Medicine entitled "The problem of pain in oncology," by Dr. H. J. Senn ("the Senn reference"). (Brown Decl., Ex. 20, at TR000326-27.) The Senn reference also discloses following the WHO Guidelines' three-step ladder for treating cancer pain. (Id. at TR000332.) Table 6 discloses what Senn "believe[s] are the most widely used drugs" for pain therapy, including acetaminophen and tramadol. (Id.) Table 7 in Senn teaches how to use these drugs in the three-step analgesic ladder. (Id.) It discloses using 0.5 to 1.0 gram of acetaminophen every four to six hours at step one, and 50 to 100 mg of tramadol every 4 to 6 hours at step two. (Id. at TR000332.) Under step two, Table 7 indicates that it is an option to combine drugs from step one by stating: "(opt. + Step 1 + Adjuvants**)." (Id.)

Fifth, Kali cites an article entitled "Analgesic Therapy in Tumor Patients in Practice," by Jochen Brinkmann ("the Brinkmann reference"). (Brown Decl., Ex. 18.) Brinkmann does not cite the WHO Guidelines, but describes a similar cancer pain treatment regimen. In the "early phase" of treatment, Brinkmann advises medicating "just with the maximum peripherally acting substances," such as acetaminophen up to one gram every 4 hours. (Id. at TR000043.) Brinkmann then

states that it is an "oncological disadvantage," that "there are few fixed combinations of analgesics on the market." (Id.) He explains that "these combinations can facilitate a reduction of the individual dosage of the components and thus reduce risk considerably." (Id.) "One way to get around this" disadvantage, the article advises, is to create combinations with individual preparations. (Id.) "If these substances [peripherally acting analgesics] alone do not suffice, there is the alternative of combining them with centrally acting analgesics," states Brinkmann. (Id.) "Tramadol," among other drugs, the reference explains, "combine[s] very well with the peripherally acting substances listed above," which include acetaminophen. (Id. at TR000044.) In an example, Brinkmann describes administering "1 g of [acetaminophen] + 40 drops[34] of Tramadol (*Tramal*®) every 4 hours +20 drops of Metoclopramid (*Paspertin*®)." (Id.)

The final prior art reference is an article entitled "Medicinal Pain Therapy," by P.J. Meier and W.H. Ziegler ("the Meier reference"). (Brown Decl., Ex. 21.) Under the heading "General Principles of Medicinal Pain Therapy," Meier introduces a table summarizing "[a] few important fundamentals of medicinal pain therapy." (Id. at TR000250.) Fundamental number five is the "[c]ombination of

[34] Forty drops contains 100 mg of Tramadol. (OMP Facts ¶ 92.)

substances with different points of attack to achieve an additive or *synergistic analgesia* and to reduce side effects." (Id. (emphasis added).) Meier goes on to describe the features of the most often used peripherally-acting "simple analgesics" such as aspirin and acetaminophen. (Id. at TR000252.) Meier states that an individual dose of acetaminophen ranges from 0.5 to 1.0 g for adults. (Id.) Thereafter, Meier describes various centrally-acting "Opiates and Opioid Analgesics," including morphine, which Meier states is the standard-bearer for the group. (Id. at TR000255-56.) After describing the features of various other centrally-acting analgesics, Meier discloses that

> *Tramadol* (Tramal®) has a structure similar to that of morphine, but in contrast to morphine causes no urinary retention and constipation. Finally, it should be mentioned again that centrally and peripherally acting analgesics in combination strengthen their pain alleviating effect due to their different points of attack (e.g., codeine and [aspirin]).

(Id. at TR000257.) In a chart demonstrating the characteristics of "some opiate and opioid analgesics," Meier states that a standard oral dose of Tramadol is 100 to 200 mg. (Id. at TR000251.)

Ortho-McNeil makes several arguments regarding what the above references would suggest to one of ordinary skill in the art. Whether prior art suggestions teach away or toward the claimed invention is a finding of fact that is

a "subsidiary requirement" of the "scope and content of the prior art" Graham factor. See Dystar Textilfarben GmbH v. C.H. Patrick Co., 464 F.3d 1356, 1360 (Fed Cir. 2006). However, for clarity's sake, the Court will separately address below what the prior art does or does not suggest in its discussion of whether Kali has presented a prima facie case of obviousness, and if so, whether Ortho-McNeil has rebutted that case.

### c. Graham Factor 3: The Differences Between the Claimed Invention and the Prior Art

As explained in their anticipation arguments, the parties dispute whether the Sorge reference and the Flick patent individually describe each limitation of Claim 6. As the Court held above, the Sorge reference fails to disclose a "pharmaceutical composition." Additionally, it is assumed here that Flick fails to disclose "about 1:5." Combined, the prior art as a whole very nearly describes every limitation of Claim 6.

#### i. Limitation 1: "Pharmaceutical Composition"

The Court has interpreted "pharmaceutical composition" to require a medicinal preparation comprising an intimate admixture, prepared outside the

body, generally in the form of a dosage unit, such as a tablet or capsule. Of the prior art cited above, only the Flick patent explicitly describes tramadol and acetaminophen as components of a single composition, combined into one tablet, and thus, in a "pharmaceutical composition." See '589 patent, col. 12, ll. 67-75. Every other reference describes only the co-administration of tramadol and acetaminophen, or the co-administration of acetaminophen and weak opioids generally.

**ii. Limitation 2: "Comprising a Tramadol Material and Acetaminophen"**

The Flick patent, and the Sorge, Beyer, Senn, Brinkmann, and Meier references all disclose administering tramadol and acetaminophen together to treat pain. Flick discloses a specific example of a pharmaceutical composition containing these two compounds, (see '589 patent, col. 12, ll. 70-75.), and Brinkmann discloses a specific example of the co-administration of these two compounds, (Brown Decl., 18, at TR000044.). Both of these examples also contain at least one additional active ingredient; however as discussed above, this does not depart from Claim 6 because the term of art "comprising" permits the

inclusion of additional elements.[35]

In addition, Sorge, Beyer, Senn, and Meier all disclose that cancer pain can be treated with the co-administration of a peripheral analgesic and a weak opioid, as taught by the WHO Guidelines, and these references all list acetaminophen and tramadol as examples of a peripherally-acting analgesic and a weak opioid, respectively, that can be used in the regimen.[36] (See Brown Decl., Ex. 17, at

[35] See supra, footnote 30.

[36] Ortho-McNeil's briefing at times suggests that the Beyer, Senn, Brinkmann, and Meier references differ from Claim 6 in that they "fail to *disclose* even the co-administration of tramadol and acetaminophen to one of ordinary skill in the art." (OMP Facts ¶ 89 (emphasis added); see also Pl.'s Opp'n Br. 36 (stating that the above references do not suggest using acetaminophen and tramadol in the WHO Guidelines regimen).) Although Ortho-McNeil uses the term "disclose," the Court understands this to be an argument that these prior art references contain no *suggestion or motivation* to combine or modify, because a person of ordinary skill, given his or her experience, would reject the prior art's express disclosures–not an argument that the references do not actually disclose what they expressly teach. See, e.g., Merck & Co. v. Biocraft Labs., Inc., 874 F.2d 804, 807-08 (Fed. Cir. 1989) (equating what a prior art reference "discloses" or "describe[s]" with what it "expressly teach[es]," and distinguishing these terms from what a prior art teaching or disclosure "would have *suggested* to one of ordinary skill," in the obviousness analysis).

The issue of what the prior art suggests to the person of ordinary skill, or motivates that person to do will be addressed below; the issue here in Graham factor three is whether there are any differences between the teachings of the prior art and the claimed invention. On the face of the Beyer, Senn, Brinkmann, and Meier references, the answer is no–they all teach a tramadol material and acetaminophen together, as does Claim 6. Indeed, this fact is acknowledged by

TR000007-08; Ex. 18, at TR000043-44; Ex. 19, at TR000056-57; Ex. 20, at TR000332; Ex. 21, at TR000250-52, TR000257.) Thus, there are no differences between the prior art and the second limitation of Claim 6.

### iii. Limitation 3: "Wherein the Ratio of the Tramadol Material to Acetaminophen is a Weight Ratio of About 1:5"

The third and last limitation of Claim 6 is a weight ratio of "about 1:5," which encompasses ratios up to and including 1:7.1 and ratios down to and including 1:3.6. Assuming Flick does not anticipate Claim 6, the administration of

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Ortho-McNeil in other portions of its briefing. (See, e.g., OMP Facts ¶ 78 ("[A] reader skilled in the art [reading the Sorge reference] could randomly arrive at separate formulations of tramadol and acetaminophen, as well as no less than 19 other combinations of a peripherally acting analgesic and a weak opioid."), ¶ 91 ("The Brinkmann reference discloses a list of four (4) opioids, including tramadol, and states that they can be combined with a list of four (4) peripherally acting analgesics, including acetaminophen.").)

The Court notes that the terms "disclose," "describe," "teach," "suggest," and "motivate" are sometimes used interchangeably by the parties here, and in some obviousness case law generally. To be clear, in this opinion's obviousness analysis, the terms "disclose," "describe," and "teach," are synonymous terms meaning what a piece of prior art expressly states. In contrast, the terms "suggest" and "motivate" are used solely to mean what the person of skill in the art would take away from reading the disclosures, descriptions and express teachings of the prior art, as this is relevant to the obviousness analysis' "motivation-suggestion-teaching test." A suggestion or motivation, of course, can "teach toward or away" from the claimed invention. See Medichem, S.A. v. Rolabo, S.L., 437 F.3d 1157, 1165 (Fed. Cir. 2006).

tramadol and acetaminophen in a weight ratio of "about 1:5" is not fully disclosed in the prior art. Flick and Brinkmann disclose 1:10. ('589 patent, col. 12, ll. 65-75; Brown Decl., Ex. 18, at TR000044.) The Sorge, Beyer, and Senn references disclose a range of 1:5 to 1:20. All three of these references describe the co-administration of acetaminophen and tramadol in the context of utilizing the WHO Guidelines' three-step cancer pain treatment ladder. In doing so, the three references describe a 500 to 1000 mg dose of acetaminophen,[37] and a 50 to 100 mg dose of tramadol. (Brown Decl., Ex. 17, at TR000006-08; Ex. 19, at TR000056-57; Ex. 20, at TR000332.) These doses combined describe a range of weight ratios spanning from 1:5 (100 mg tramadol/500 mg acetaminophen), to 1:20 (50 mg/1000 mg), partially overlapping 1:3.6 to 1:7.1. The Meier reference discloses a range of 1:2.5 to 1:10. That reference also employs a 500 to 1000 mg dose of acetaminophen in the context of the WHO Guidelines three-step plan, but discloses a higher, 100 to 200 mg oral dose of tramadol. (Id. ex. 21, at TR000251-52, TR000256-57.) Those doses combined create a 1:2.5 (200 mg/500 mg) to 1:10 (100 mg/1000 mg) range, fully overlapping the 1:3.6 to 1:7.1 range of "about 1:5."

[37] The Senn and Meier references disclose a 0.5 to 1.0 gram dose of acetaminophen, which is the equivalent of 500 to 1000 mg.

Ortho-McNeil, relying on the opinion of Dr. Stanski, claims that the dosing ranges described in Sorge are only relevant to administering either tramadol or acetaminophen alone, and not when co-administered with each other. (See, e.g., OMP Facts ¶ 79 (citing Stanski Val. Rep ¶ 59, and Brown Decl., Ex. 17, at TR000008).) The dosages disclosed in Sorge are described as "individual dosages," but neither Ortho-McNeil nor Dr. Stanski can point to any language stating that these doses are not relevant to using peripherally acting analgesics and weak opioids in combination. Dr. Stanski merely offers the conclusory assertion that "the doses provided in the tables in Sorge pertain to administration of single-agent drugs, not doses of drugs that have multiple active ingredients." (Stanski Val. Rep. ¶ 59.) He cites no support in the record for such an assertion, and indeed, there is none. Instead, Dr. Stanski claims that "[t]here is nothing in the reference suggesting to one of ordinary skill that the same amount of drug would be used if" the two drugs were administered together. (Id.) To the contrary, shortly after disclosing the tramadol and acetaminophen doses, Sorge states that "[i]f a sufficient analgesia is attained under a specific daily dosage of an opiate, but pain spikes continue to occur at irregular intervals, it is possible to administer

an additional pain killer as needed," such as "a peripheral pain killer," used "[a]s a sort of 'top-up analgesic.'" (Brown Decl., Ex. 17, at TR000009.) The only "daily dosage" of opiate Sorge could possibly be talking about here are the "individual dosage[s]" listed just lines earlier, which Ortho-McNeil claims are only relevant to single-agent administrations. However, Sorge clearly states that an additional peripheral pain killer can be added to this opioid dose. This disclosure undercuts Ortho-McNeil's reading of Sorge. Indeed, the more rational reading of Sorge (and of Beyer, Senn, and Meier), is that the dosages should be presumed to be applicable to using the drugs alone or in combination, because all four references teach both uses, and all four only teach one set of dosages, without expressly stating that those dosages are relevant only to single-agent, or double-agent administrations. The Court finds it highly unlikely that all four references simply omitted listing special dosages relevant only to peripheral and weak opioid analgesic combinations. The portion of Sorge quoted above, which is not addressed by Ortho-McNeil, supports this conclusion.

Furthermore, Ortho-McNeil fails to explain how its reading of the prior art is consistent with the Senn reference's disclosure of its dosages, which are

identical to those in Sorge and Beyer. Senn's Table 7 is entitled "[a]nalgesic ladder for drugs used in pain therapy in tumor patients," which Senn describes as "closely related to the one proposed by the WHO [Guidelines]." (Brown Decl., Ex. 20, at TR 000332.) At step one, Table 7 lists acetaminophen as an option in the same 500 to 1000 mg dose described by Sorge, Beyer, and Meier. (Id.) At step two, Table 7 lists tramadol as an option at a dose of 50 to 100 mg, also as Sorge and Beyer do. (Id.) Just below Table 7's list of step-two weak opioids appears the line: "(opt. + Step 1 + Adjuvants**)," disclosing the option of combining the drugs of step two with those of step one. (Id.) This disclosure mirrors that of the WHO Guidelines, Sorge, Beyer, and Meier, which all also describe combining step one and step two drugs. Clearly then in Senn, the 500 to 1000 mg of acetaminophen, and 50 to 100 mg of tramadol doses are relevant to the co-administration acetaminophen and tramadol. Otherwise, it would make little sense for Senn to list those doses in a table describing the WHO Guidelines regimen, and to fail to list alternate doses for step one plus step two combination regimens. Ortho-McNeil and its experts also fail to address this aspect of the prior art, and thus, the Court has no trouble finding that the acetaminophen and

tramadol dosages disclosed in Sorge, Beyer, Senn, and Meier are relevant to their teachings to administer acetaminophen and tramadol in combination.

It is not contested that if the prior art's dosing options are relevant to a combination regimen, those dosing ranges inherently disclose all weight ratios that could be created by combining the two sets of doses.[38] Cf. Titanium Metals Corp. of Am. v. Banner, 778 F.2d 775, 777, 781 (Fed. Cir. 1985) (finding that a prior art article disclosing alloy ingredient weights as graph data points disclosed the ingredient percentages that could be calculated from those data points). Moreover, despite Ortho-McNeil's suggestions to the contrary (see OMP Facts ¶ 79), the fact Sorge, Beyer, Senn, and Meier do not describe a "pharmaceutical composition," (as Flick does), does not change the fact that those references describe using tramadol and acetaminophen in weight ratios ranging from 1:5 to 1:20 and 1:2.5 to 1:10. The method of administration of the drugs, and the weight ratio of the drugs are separate limitations of Claim 6.

In sum, the weight ratios described in the prior art differ from Claim 6's "about 1:5" range, i.e., 1:3.6 to 1:7.1, in minor ways. Flick discloses exactly 1:10.

[38] (See, e.g., OMP Facts ¶ 86 (arguing that, at best, Sorge teaches using doses "that correspond to weight ratios that range from 1:20 and 1:10").

Brinkmann discloses exactly 1:10. Sorge, Beyer, and Senn disclose 1:5 to 1:20, partially overlapping "about 1:5." Meier discloses 1:2.5 to 1:10, which completely overlaps "about 1:5." These are the only differences between the claimed invention and the prior art.

**d. Prima Facie Obviousness: The Motivation-Suggestion-Teaching Test**

"It is not enough for a party seeking to defeat a patent on obviousness grounds to merely identify each element of the invention in the prior art." Janssen Pharmaceutica N.V. v. Mylan Pharms., Inc., 456 F. Supp. 2d 644, 655 (D.N.J. 2006) (citing In re Kahn, 441 F.3d 977, 986 (Fed. Cir. 2006)). The elements of nearly every invention can be identified in the prior art. Id. Instead, a prima facie case of obviousness requires the Court to apply the so-called motivation-suggestion-teaching test to the findings of the first three Graham factors. Kahn, 441 F.3d at 986-87; In re Mayne, 104 F.3d 1339, 1341 (Fed. Cir. 1997).

A patent can be obvious in light of a single prior art reference, see, e.g., B.F. Goodrich Co. v. Aircraft Braking Sys. Corp., 72 F.3d 1577, 1582 (Fed. Cir. 1996), or a combination of multiple prior art references, see, e.g., In re Geiger, 815 F.2d

686, 688 (Fed. Cir. 1987). In either case, the motivation-suggestion-teaching test requires the Court to determine whether (1) a person of ordinary skill in the art at the time of the invention, with no knowledge of the claimed invention, would have some suggestion or motivation to either modify the teachings of a single prior art reference, or to combine multiple prior art references in order to achieve the claimed invention, and, (2) in either case, reasonably expect to be successful in doing so. See Dystar, 464 F.3d at 1360; Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc., 424 F.3d 1293, 1321 (Fed. Cir. 2005); Akamai, 344 F.3d at 1195-96; SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp., 225 F.3d 1349, 1356 (Fed. Cir. 2000).

This suggestion or motivation may be derived from the teachings of the prior art reference or references themselves. SIBIA Neurosciences, 225 F.3d at 1356; Akamai, 344 F.3d at 1196. It may also be derived "from the knowledge of one of ordinary skill in the art, or from the nature of the problem to be solved." SIBIA Neurosciences, 225 F.3d at 1356 (citations omitted). The prior art need not contain an express suggestion to modify or combine to achieve the claimed invention; it "may be implicit from the prior art as a whole." In re Kotzab, 217

F.3d 1365, 1370 (Fed. Cir. 2000).

The purpose of the motivation-suggestion-teaching test inquiry is to "prevent[] statutorily proscribed hindsight reasoning when determining the obviousness of an invention." Alza Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1290 (Fed. Cir. 2006). Section 103(a) requires that the subject matter be obvious "at the time the invention was made." Thus, requiring a suggestion to modify or combine prevents the party seeking to prove obviousness from impermissibly "piec[ing] the invention together using the patented invention as a template." Texas Instruments v. United States ITC, 988 F.2d 1165, 1178 (Fed. Cir. 1993).

To show a prima facie case of obviousness here, Kali must identify either (A) a suggestion or motivation for the person of ordinary skill in the art to modify Flick's tramadol/acetaminophen pharmaceutical composition from a 1:10 weight ratio to "about 1:5," and thus, achieve the claimed invention, or (2) a suggestion or motivation for that person to combine Flick with the Sorge, Beyer, and Senn references' 1:5 to 1:20 weight ratio ranges, or the Meier reference's 1:2.5 to 1:10 weight ratio range, to achieve "about 1:5," and thus, the claimed invention.

The Court stresses that it is *not* necessary for Kali to demonstrate a suggestion or motivation to use tramadol and acetaminophen together in the first place. Numerous single prior art references already indisputably teach using these drugs together to achieve analgesia.[39] This fact distinguishes this case from Knoll Pharm. Co., Inc. v. Teva Pharms USA, Inc., 367 F.3d 1381 (Fed. Cir. 2004), which Ortho-McNeil cites for support. In Knoll, the allegedly obvious claims disclosed a pharmaceutical composition of hydrocodone, an opioid, and ibuprofen, an NSAID, combined at various weight ratios. The issue before the Federal Circuit was whether it was obvious to combine hydrocodone and ibuprofen *at all*, in any weight ratio, in view of prior art that taught combining opioids with NSAIDs generally. See id. at 1383-84. Unlike here, the prior art in Knoll did not already explicitly teach combining the two active ingredients at issue. See id. at 1384; Knoll Pharm. Co., Inc. v. Teva Pharms. USA, Inc., 2002 U.S. Dist. LEXIS 17201, at *40 (N.D. Ill. Sept. 12, 2002).

[39] (See Part II.C.2.b., supra (discussing Graham Factor 2); '589 patent, col. 12, ll. 66-75; Brown Decl., Ex. 17, at TR000005-08 (Sorge); Ex. 19, at TR000056-57 (Beyer); Ex. 20, at TR000332 (Senn); Ex. 18, at TR000043-44 (Brinkmann); Ex. 21, at TR000252, TR000255-56) (Meier); see also Brown Decl., Ex. 13, at KAL016428-29, KAL016459 (explaining that combinations of non-opioids and opioids "produce additive analgesic effects . . . and are often used") (WHO Guidelines)).

Furthermore, it is also not necessary for Kali to identify a suggestion or motivation to put a tramadol and acetaminophen combination into a pharmaceutical composition, such as a tablet. Flick already anticipates these limitations.[40] Accordingly, the distinct issue in this case is whether there is a suggestion or motivation to take Flick's pharmaceutical composition of tramadol and acetaminophen, and either modify it, or combine it with other prior art, in order to achieve the "about 1:5" weight ratio.

### i. Prong 1: Suggestion or Motivation to Combine or Modify the Prior Art to Achieve the Claimed Invention

Ortho-McNeil argues that Kali cannot establish a case of prima facie obviousness because the prior art contains no suggestion or motivation to use an

[40] This fact distinguishes this case from Richardson-Vicks Inc. v. The Upjohn Co., 122 F.3d 1476 (Fed. Cir. 1997), relied upon by Kali. There, the claim accused of obviousness disclosed a pharmaceutical composition comprising ibuprofen and pseudoephedrine in weight ratios ranging from about 1.5:1 to about 8:1. Id. at 1480. The issue was "whether one of ordinary skill in the art would have combined the two ingredients into *a single form*," over prior art disclosing, *inter alia*, that doctors regularly prescribed the *co-administration* of ibuprofen and pseudoephedrine. Id. at 1480-81 (emphasis added). Unlike here, the prior art in Richardson-Vicks did not already explicitly teach administering a combination of the two active ingredients at issue *in a pharmaceutical composition*, such as a tablet. Id. at 1481.

"about 1:5" weight ratio in order to achieve synergy between tramadol and acetaminophen. (Pl.'s Opp'n Br. 34.) Kali argues that it need not demonstrate a suggestion of synergy at "about 1:5" in the prior art because there is so slight a difference between Claim 6's "about 1:5" ratio and the ratios disclosed in the prior art that Claim 6 is presumptively prima facie obvious. (Kali's Br. 22-23.)

The Court agrees with Kali. "'[W]hen the difference between the claimed invention and the prior art is the range or value of a particular variable, then a prima facie rejection is properly established when the difference in range or value is minor,'" Ormco Corp. v. Align Tech., Inc., 463 F.3d 1299, 1311 (Fed. Cir. 2006) (alteration in original) (quoting Haynes Int'l, Inc. v. Jessop Steel Co., 8 F.3d. 1573, 1577 n. 3 (Fed. Cir. 1993)), or where the claimed range overlaps or touches the range recited in the prior art, id. (citing In re Geisler, 116 F.3d 1465, 1469 (Fed. Cir. 1997), and In re Malagari, 499 F.2d 1297, 1303 (C.C.P.A. 1974)). In such cases, "[t]he normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." In re Peterson, 315 F.3d 1325, 1330 (Fed. Cir. 2003); In re Boesch, 617 F.2d 272,

276 (C.C.P.A. 1980) ("Discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." (citations omitted)).[41] As a result, the claim is presumptively prima facie obvious. See, e.g., Haynes, 8 F.3d at 1577 & n.3.

**(a) Suggestion to Modify the Flick Patent**

Claim 6 differs from the Flick patent only in that the latter discloses a 1:10 tramadol to acetaminophen weight ratio instead of "about 1:5." The Federal Circuit has found similarly small differences between variables to be prima facie obvious "where one would have expected them to have the same properties." Peterson, 315 F.3d at 1329 (citing Titanium Metals, 778 F.2d at 783).

In Titanium Metals, the Federal Circuit held invalid for obviousness a claim to an alloy composed of 0.3% molybdenum ("Mo") and 0.8% nickel ("Ni") over prior art disclosing alloys containing both 0.25% Mo and 0.75% Ni, and 0.31% Mo and 0.94% Ni. 778 F.2d at 783. "The proportions are so close," the Court

[41] See also Gentiluomo v. Brunswick Bowling & Billiards Corp., 36 Fed. Appx. 433, 438 (Fed. Cir. 2002) (not published) (explaining that "in cases in which the claimed invention differs from the prior art only in that the claims recite a range of values for a variable different from the range disclosed in the prior art," that "the invention would have been prima facie obvious because an ordinarily skilled artisan would have sought the optimum values for the variable").

explained, "that prima facie one skilled in the art would have expected them to have the same properties." Id.

Similarly in Merck & Co., Inc. v. Biocraft Labs., Inc., 874 F.2d 804, 805-06 (Fed. Cir. 1989), the claimed invention (the '430 patent) disclosed a composition of two types of diuretic, amiloride and hydrochlorothiazide, combined at a 1:10 weight ratio. A prior art patent (the '813 patent) disclosed combining amiloride with a large class of drugs that included hydrochlorothiazide. Id. Like here, the patent holder argued nonobviousness on the basis of its claimed invention's dosage limitation, which was not disclosed by the prior art patent. Id. at 806, 809. Indeed, the prior art '813 patent in Merck contained no weight limitation at all. Id. at 807. Nevertheless, the patent examiner found the claimed invention prima facie obvious, id. at 806, 808, and the Federal Circuit agreed, pointing out that "'[n]ormally it is to be expected that a change in temperature, or in concentration, or both, would be an unpatentable modification,'" id. at 809 (quoting In re Aller, 220 F.2d 454, 456 (C.C.P.A. 1955)). The Federal Circuit then required the patent holder to point to unexpected results at its claimed weight of the combination in

order to demonstrate patentability. See id. at 809.[42]

Here, the difference between Claim 6's "about 1:5," i.e., 1:3.6 to 1:7.1, and Flick's exactly 1:10 is sufficiently small to render Claim 6 prima facie obvious. Indeed, the difference is much smaller than that which existed in Merck v. Biocraft Laboratories. The difference is so slight that not only would one skilled in art expect them to have the same analgesic properties, Ortho-McNeil and its expert expected them to have the same properties. Ortho-McNeil asserted in its doctrine

[42] See also In re Huang, 100 F.3d 135, 137, 139 (Fed. Cir. 1996) (finding a claim to a shock-absorbing tennis racquet grip composed of a textile layer and a polyurethane layer with a thickness ratio "equal to or larger than approximately 0.18" obvious over prior art disclosing the same two layers in thickness ratios ranging from 0.111 to 0.142 because "one of ordinary skill would logically infer that increasing the amount of the shock absorbing material . . . would lead to an increase in the amount of shock absorption.[] Accordingly, one of ordinary skill would have experimented with various thicknesses to obtain an optimum range"); In re Hill, 284 F.2d 955, 959 (C.C.P.A. 1960) (finding a claim to a chemical process performed at 150-250 degrees obvious over prior art describing the same process and result at 300 degrees, because this difference "represents an unpatentable variation over the prior art and since the other features of claims 1-5 are taught by the references, the feature which is not shown cannot render the claims patentable because it is not itself unobvious"); In re Aller, 220 F.2d 454, 825-27, 830 (C.C.P.A. 1955) (finding prima facie obvious a claim to a chemical process disclosing use of 25-70% sulfuric acid at 100 degrees over prior art describing same process using 10% sulfuric acid at 100 degrees because "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation").

of equivalents argument, through the report of Dr. Stanski, that there is "an insubstantial difference in potency of an analgesic Tramadol:[acetaminophen] pharmaceutical composition having a weight ratio of 1:5 relative to one having a weight ratio of 1:8.67." (Stanski Inf. Rep. at p. 12, ¶ 28). And as the District Court for the Eastern District of Michigan pointed out while examining the identical doctrine of equivalents issue in Caraco, "[t]here is no basis to say that the ratio of 'about 1:5' is equivalent to a ratio of 1:8.67, but not to 1:10." 2005 U.S. Dist. LEXIS 24998, at *15. Moreover, although it is not prior art, the Court notes that the '691 patent's specification represents that its experimental data "establishes that compositions having a ratio of tramadol to [acetaminophen] from 1:1 to 1:1600 . . . give unexpectedly enhanced activity . . . ." '691 patent, col. 8, ll. 64-70.

Given the slight difference between the claimed range and Flick's 1:10, the Court concludes that one of ordinary skill in the art working from the Flick patent would be presumed to have been motivated to seek the optimum values for the weight ratio variable. Cf. Peterson, 315 F.3d at 1330.

**(b) Suggestion to Combine Flick with the Sorge, Beyer, Senn or Meier References**

Kali has also demonstrated a prima facie case that Claim 6 is obvious over Flick in view of the Sorge, Beyer, Senn, and Meier references, which all disclose a range of tramadol to acetaminophen weight ratios that either partially or fully overlap "about 1:5." As mentioned above, "[a] prima facie case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." Peterson, 315 F.3d at 1329 (citing Geisler, 116 F.3d at 1469). For example, in Geisler, the patent applicant's claim described a reflective article with a three-layer coating. 116 F.3d at 1467. The third layer was an outer, protective layer "50 to 100 Angstroms thick." Id. The patent applicant *conceded*, and the Federal Circuit agreed, that its claim was prima facie obvious over two prior art references: (1) the Wagner reference, which disclosed a three-layer reflective coating, but without a specified thickness for the outer layer, and (2) the Zehender patent, which disclosed only a two-layer reflective coating, but with an outer, protective layer 100 to 600 Angstroms thick. Id. at 1467-68. Combined, the only difference between the two prior art references and the claim was the claimed thickness ranges, which overlapped partially at their endpoints of 100 Angstroms. Id. at 1469.

Nearly identically here, (1) the Flick patent discloses a pharmaceutical composition comprised of tramadol and acetaminophen, but without the claimed weight ratio, and (2) Sorge, Beyer, and Senn disclose only the co-administration of tramadol and acetaminophen, but do so in weight ratios of 1:5 to 1:20. Combined, the prior art contains the first two limitations of Claim 6, and overlaps "about 1:5" from 1:5 to 1:7.1. Thus, Claim 6 is obvious over Flick in view of Sorge, Beyer, and Senn.

Claim 6 is also prima facie obvious over Flick in view of Meier, whose 1:2.5 to 1:10 range fully overlaps and is broader than Claim 6's 1:3.6 to 1:7.1 range. The Federal Circuit has explained that

> [s]electing a narrow range from within a somewhat broader range disclosed in a prior art reference is no less obvious than identifying a range that simply overlaps a disclosed range. In fact, when, as here, the claimed ranges are *completely encompassed by the prior art*, the conclusion is *even more compelling* than in cases of mere overlap.

Peterson, 315 F.3d at 1330 (emphases added). Accordingly, Claim 6 is prima facie obvious because the person of ordinary skill would be motivated to combine references in order to "'discover the optimum or workable ranges by routine experimentation.'" Geisler, 116 F.3d at 1470 (quoting Aller, 220 F.2d at 456).

### ii. Reasonable Expectation of Success

The second prong of the motivation-suggestion-teaching test requires "that a skilled artisan would have perceived a reasonable expectation of success in making the invention via that combination." Medichem, S.A. v. Rolabo, S.L., 437 F.3d 1157, 1165 (Fed. Cir. 2006). Ortho-McNeil argues that only the existence of safety and efficacy data in the prior art for tramadol and acetaminophen at "about 1:5," could provide a reasonable expectation of success because, "without clinical data, one would not have been able to know the safety and efficacy of [the] composition." (Pl.'s Supp. Opp'n Br. at p. 15.) However, a reasonable expectation of success does not require *absolute* predictability of success. In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988). It requires only that

> one must be motivated to do more than merely to "vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful."

Medichem, 437 F.3d at 1165 (quoting O'Farrell, 853 F.2d at 903).

Here, the Court finds that a reasonable expectation of success has been established. Where the only difference between the prior art and the claimed

invention is the value of a claimed variable, the Federal Circuit has found small differences between ranges, or overlap between the ranges, dispositive as to prima facie obviousness without requiring an additional showing to satisfy the reasonable expectation of success prong. See, e.g., Medichem, 437 F.3d at 1167-68 (reasonable expectation of success found where claimed range was "entirely within the range of the prior art"); Peterson, 315 F.3d at 1329-30; Geisler, 116 F.3d at 1469; In re Huang, 100 F.3d 135, 138-39 (Fed. Cir. 1996); Merck, 874 F.2d at 809 (reasonable expectation of success found where only difference between claim and prior art was the absence of the claimed range); Malagari, 499 F.2d at 1303; Aller, 220 F.2d at 826-30. The similarities or overlap between the claimed range and the prior art gives an indication of which parameters are critical and thus makes it reasonable to expect that routine experimentation will result in the claimed range. That is, it provides a reasonable expectation of success. See, e.g., Pfizer, Inc. v. Apotex, Inc., No. 06-1261, 2007 U.S. App. LEXIS 6623, at *50-54 (Fed. Cir. March 22, 2007) (finding a reasonable expectation of success where the optimum acid addition salt was easily ascertainable via routine experimentation, analogizing to cases involving "the optimization of a range or

other variable," citing Peterson, 315 F.3d at 1330, Geisler, 116 F.3d at 1470, Merck, 874 F.2d at 809, and Aller, 220 F.2d at 456).

Furthermore, as explained in detail below, the prior art revealing ranges that overlap or encompass "about 1:5," also teach towards "about 1:5" within those disclosed ranges. Thus, this is not a case "'where the prior art g[ives] either no indication of which parameters [are] critical or no direction as to which of many possible choices is likely to be successful.'" See Medichem, 437 F.3d at 1165 (quoting O'Farrell, 853 F.2d at 903).

In sum, the Court finds that a reasonable fact finder would conclude that Kali has pointed to clear and convincing evidence demonstrating a prima facie case of obviousness. This showing now "shifts the burden to the [patent holder] to show that his invention would not have been obvious." See Peterson, 315 F.3d at 1330.

### e. Rebuttal of the Prima Facie Case

#### i. Unexpected Results

There are two ways in which Ortho-McNeil can rebut Kali's prima facie case. First, it can show that the "claimed range[] 'produces a new and unexpected

result which is different in kind and not merely in degree from the results of the prior art." Huang, 100 F.3d at 139 (quoting Aller, 220 F.2d at 456).

**(a) Synergy**

Ortho-McNeil first argues that Claim 6 demonstrates unexpected results because its composition is synergistic. That Claim 6 possesses synergism is not disputed, and indeed is supported by the test results in the '691 patent specification. See '691 patent, col 7, l. 46-col. 8, l. 68. However, Ortho-McNeil fails to demonstrate that this result is new or unexpected in view of the prior art. Specifically, the Flick patent, Brinkmann reference, and Meier reference all teach that combining acetaminophen and tramadol will, or is likely to, result in synergistic effects.

The Flick patent teaches synergy in the context of its use-in-combination teaching. The specification states in example 22 that

> [Tramadol has] also proven to be of considerable therapeutic value *when used in combination with other therapeutically active agents whereby frequently a synergistic effect is observed*. Especially valuable combinations are those *with other analgesics* such as with acetylsalicylic acid, phenacetin, or the like; [and with antiphlogistic and anti-inflammatory agents, analeptics, antihistaminic agents, spasmolytic agents, muscle relaxants, and sedatives].

> The following example [#23] *illustrates the composition of such combination preparations* without, however, limiting the same thereto.

'589 patent, col. 12, ll. 45-64 (emphases added). Example 23 then follows, disclosing a pharmaceutical composition comprised of tramadol and acetaminophen in a weight ratio of 1:10. '589 patent, col. 12, ll. 66-75. Thus, Flick clearly teaches that "frequently a synergistic effect is observed" from combining tramadol with "analgesics," such as acetaminophen.

Ortho-McNeil claims that the person of ordinary skill in the art would disregard these teachings. First, relying on the expert report of Dr. Stanski, Ortho-McNeil claims that Flick's example 23 would not exhibit synergy if created. (Pl.'s Opp'n Br. 47 (citing Stanski Val. Rep. ¶ 94).) However, Dr. Stanski's opinion does not result from an allegation that tramadol and acetaminophen fail to exhibit synergy when combined at a 1:10 weight ratio as opposed to "about 1:5." Instead, Dr. Stanski claims that Flick's inclusion of the active ingredient, pentobarbital sodium in example 23 would negate any analgesic synergism resulting from the combination of tramadol and acetaminophen. (Stanski Val. Rep. ¶ 94.) True or not, this fact is immaterial. The question here is whether unexpected results occur

from using "about 1:5" instead of 1:10, not whether subtracting an extraneous agent from example 23 creates unexpected results. See Geisler, 116 F.3d at 1469-70 (stating that a prima facie case may be rebutted "by showing that the claimed *range* achieves unexpected results relative to the prior art *range*" (emphases added) (internal quotations omitted)). The latter question is relevant only to Claim 6's "*comprising* a tramadol material and acetaminophen" limitation—a limitation that Ortho-McNeil concedes that Flick fully discloses. As touched upon above, by using the term of art "comprising," Claim 6 allows for the addition (and subsequent subtraction) of additional active ingredients to its tramadol/acetaminophen combination. Thus, even if, as Dr. Stanski claims, adding pentobarbital sodium to a tramadol/acetaminophen combination negates example 23's synergism, this fact is also true for Claim 6, and accordingly does not represent a true difference in kind between example 23 and Claim 6. It follows then that Dr. Stanski's opinion does not create a genuine issue of fact as to the existence of unexpected results from using "about 1:5" instead of 1:10. Indeed, Dr. Stanski's opinion that example 23 and its 1:10 weight ratio would not be synergistic *only* because of the presence of pentobarbital sodium, implies that

example 23 would be synergistic without it–an implication that is confirmed by Flick's own synergy teaching.

Second, relying again on Dr. Stanski's validity report, Ortho-McNeil attacks the Flick patent's claim to synergy as scientifically implausible, and thus, bound to be disregarded by the person of ordinary skill. Dr. Stanski's opinions on this issue do not fully support what Ortho-McNeil cites them for, however. Dr. Stanski's validity report never states that the person of ordinary skill would find implausible Flick's claim that a combination of tramadol with an analgesic, like acetaminophen in example 23, would frequently exhibit synergy. Instead, he criticizes Flick for not limiting its broad claim to synergism to analgesics. He states that

> Flick's suggestion regarding "synergy" *is not limited to analgesic combinations*, but applies to the combination of Tramadol with not only a wide range of active ingredients, but to entirely different therapeutic classes of active ingredients, ie anti-histamines, sedatives etc. To suggest that *each of those active ingredients* in combination with Tramadol would exhibit "synergistic" interactions is scientifically unrealistic.

(Stanski Val. Rep. ¶ 91 (emphases added).) That Dr. Stanski took the time to stress that Flick's synergy suggestion is "not limited to analgesic combinations,"

implies that "each of those active ingredients" does not refer to analgesics, but only to "entirely different therapeutic classes of active ingredients." Even if he was referring to analgesic combinations as well, Dr. Stanski only opines that it is unrealistic to expect *each* member of this broad array of active ingredients to be synergistic in combination with tramadol, not that it is unrealistic to expect *any* of them to do so. In light of these premises, his ultimate conclusion a few lines later that Flick therefore "would have provided [a person of ordinary skill in the art] with no motivation to prepare a pharmaceutical composition of Tramadol and [acetaminophen] at a weight ratio of about 1:5," is itself overbroad, and does not follow. In any event, the only "fact" Dr. Stanski cites to support this opinion is that "[t]o [his] knowledge, in 1972 when the '589 patent issued, there were few, if any, pharmaceutical combinations that had been proven to produce a synergistic effect." (Stanski Val. Rep. ¶ 91.) He cites no prior art references, articles, patents, or documentary evidence of any kind in the record supporting this claim, and thus, even if his conclusory opinion were on point, it would not create a genuine issue of fact defeating summary judgment. See, e.g., Novartis, 271 F.3d at 1051.

Importantly, Flick's teaching of synergy between tramadol and analgesics

like acetaminophen is not tied to the use of any specific weight ratio. Flick is explicit that example 23 and its 1:10 weight ratio is merely a non-limiting illustration of the use-in-combination and synergy teachings. Therefore, Flick teaches that synergy results from *any* combination of tramadol and acetaminophen, further undermining Ortho-McNeil's claim that synergy at "about 1:5" was unexpected. In an analogous situation in Merck, 874 F.2d at 807, 809, the patent holder there argued that its claimed amiloride/hydrochlorothiazide composition was nonobvious because it possessed the unexpected result of reducing the excretion of potassium ions when administered in its claimed 1:10 weight ratio. The Federal Circuit disagreed, citing a prior art patent teaching that a reduction of the excretion of potassium ions results when amiloride is combined with a class of compounds including hydrochlorothiazide. Id. This teaching was not tied to the use of the two drugs in any particular weight ratio. Id. Thus, the Court concluded that reduction of the excretion of potassium ions was already "to be expected from the known . . . properties of the two [drugs]." Id. at 809. The facts here are indistinguishable, and accordingly, the Court finds that Ortho-McNeil has failed to demonstrate that Claim 6's synergism is an unexpected result relative to the Flick

patent.

In addition to Flick's teaching, the Brinkmann reference also suggests synergy results at a tramadol to acetaminophen weight ratio of 1:10, providing further evidence that synergy at "about 1:5" is neither new or unexpected relative to the prior art. Brinkmann teaches that analgesic combinations "facilitate a reduction of the individual dosage of the components and thus reduce the risk [of side effects] considerably." (Brown Decl., Ex. 18, at TR000043.) This is a feature of synergy (Stanski Inf. Rep. ¶ 35), that Ortho-McNeil claims makes Ultracet unique (Pl.'s Opp'n Br. 36, 39.). Brinkmann then goes on to suggest combining tramadol with acetaminophen, and gives a specific example of the two drugs in a 1:10 weight ratio combination. (Id. at TR000043-44.)

Finally, and even more explicitly, the Meier reference also suggests that synergy occurs in tramadol/acetaminophen combinations ranging from weight ratios of 1:2.5 to 1:10. Meier states that it is a "fundamental[] of medicinal pain therapy," to combine "substances with different points of attack to achieve an additive or *synergistic analgesia* and to reduce side effects." (Brown Decl., Ex. 21, at TR000250 (emphasis added).) After describing acetaminophen as a

peripherally-acting analgesic dosed from 500 to 1000 mg (Id. at TR000252), and tramadol as a centrally-acting analgesic, similar to, but in some ways better than, morphine, and dosed from 100 to 200 mg, (Id. at TR000251, 257), Meier stresses again "that centrally and peripherally acting analgesics in combination *strengthen their pain alleviating affect* due to their different points of attack," (Id. at TR000257 (emphasis added).).

Ortho-McNeil and its experts give no explanation how, in light of these teachings by Brinkmann and Meier, the synergy resulting at "about 1:5" was unexpected over the prior art. Ortho-McNeil simply asserts that "[n]one of the [prior art] publications even indirectly suggests that there is a synergistic analgesic effect between tramadol and acetaminophen that might be exploited to reduce doses of these two drugs in a combination regimen." (Pl.'s Opp'n Br. at p. 36.) In light of Flick, Brinkmann, and Meier's synergy teachings, no rational finder of fact could agree with this statement. Dr. Stanski's validity report does not dispute that Brinkmann contains an example of using tramadol and acetaminophen in a weight ratio of 1:10, but he fails to acknowledge Brinkmann's teaching that analgesic combinations "facilitate a reduction of the individual dosage of the components

and thus reduce the risk [of side effects] considerably," a feature which Dr. Stanski himself states is indicative of synergism in his infringement report. (See Stanski Inf. Rep. ¶ 35.) Dr. Stanski only takes issue with Brinkmann's failure to teach a "pharmaceutical composition" (Stanski Val. Rep. ¶¶ 71-73), a limitation not at issue here. As to Meier, Dr. Stanski similarly ignores its explicit synergism teachings, and offers nothing more than conclusory and immaterial allegations that the article does not render Claim 6 obvious because it does not teach a "pharmaceutical composition." (Stanski Val. Rep. ¶¶ 74-77.)

**(b) Other Alleged Unexpected Results**

Finally, in addition to synergy, Ortho-McNeil offers other alleged unexpected results, including: a faster onset of action, a longer lasting analgesia, effectiveness in new pain settings, fewer side effects, and all while using 25 percent less tramadol than tramadol-only drugs. There are two problems with this group of alleged unexpected results that make them immaterial to the issue at hand. First, Ortho-McNeil alleges that these are all unexpected results of "Ultracet," not of the Claim 6 composition. (Pl.'s Opp'n Br. at p. 39.) "For objective evidence to be accorded substantial weight, its proponent must establish

a nexus between the evidence and the merits of the *claimed* invention." In re GPAC Inc., 57 F.3d 1573, 1580 (Fed. Cir. 1995) (emphasis added) (citing Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 1539 (Fed. Cir. 1983)). Ultracet, of course, has a weight ratio of 1:8.67, which lies outside the scope of Claim 6's "about 1:5" weight ratio. Thus, there is no nexus between the alleged unexpected results of Ultracet and the claimed invention.

Second, even if there were a nexus between the unexpected results alleged above and Claim 6, Ortho-McNeil only alleges that the results are unexpected features of using tramadol and acetaminophen together generally, as opposed to using tramadol alone, or acetaminophen alone. As explained earlier, the inquiry in this case is not whether using tramadol and acetaminophen in combination is nonobvious over the prior art; the issue is whether using an "about 1:5" weight ratio exhibits unexpected results, making about 1:5's use nonobvious over prior art that teaches 1:10, 1:5 to 1:20, and 1:2.5 to 1:10. Ortho-McNeil does not allege that Ultracet has a faster onset of action, a longer lasting analgesia, effectiveness in new pain settings, fewer side effects, and uses less tramadol because Claim 6 employs an "about 1:5" weight ratio instead of those revealed in the prior art.

Only such evidence could demonstrate the nonobviousness of Claim 6.

In conclusion, the Court finds that Ortho-McNeil has failed to present evidence of unexpected results such that a reasonable person could find that it has rebutted Kali's prima facie case.

### ii. Whether the Prior Art Teaches Away From the Claimed Range

The second way in which a party can rebut a prima facie case of obviousness is to "show 'that the [prior] art in any material respect taught away' from the claimed invention." Geisler, 116 F.3d at 1469 (quoting Malagari, 499 F.2d at 1303). "When a piece of prior art 'suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant' the piece of prior art is said to 'teach away' from the claimed invention." Medichem, 437 F.3d at 1165 (quoting In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994)).

Ortho-McNeil claims that the prior art teaches away from using "about 1:5" in four ways. First, in an argument already rejected above, Ortho-McNeil claims that the Flick patent's example 23 tablet would not be synergistic.

Second, Ortho-McNeil argues that "there is no motivation in Flick to alter the amounts of the agents in [example 23's] tablet to arrive at a composition within the scope of claim 6." (Pl.'s Opp'n Br. at 47.) The Court has already rejected this argument in its anticipation analysis above. But in any event, the argument misses the point. The issue here is whether the prior art *teaches away* from using "about 1:5," not whether it fails to teach toward "about 1:5." Where, as here, the claimed invention contains only a minor difference from the prior art in the range or value of a particular variable it is *presumed* that the person of ordinary skill would be motivated to find the optimum value of the variable, see, e.g., Ormco Corp., 463 F.3d at 1311; Boesch, 617 F.2d at 276, and therefore, an additional suggestion teaching towards the claimed variable or range is not needed. Only evidence that the prior art teaches in the opposite direction can effectively rebut this presumption. See e.g., Peterson, 315 F.3d at 1332 (rejecting that a prior art reference taught away from a claimed alloy containing rhenium, because, "[w]hile it mentions a preferred alloy that does not contain rhenium, it does not *disparage* or *otherwise discourage* the use of alloys containing rhenium" (emphases added)).

Ortho-McNeil's third argument is that "a person of skill would read Sorge[, the WHO Guidelines, Beyer, Senn, Brinkmann, and Meier] to discourage (*i.e.*, teach away from) fixed ratio, single formulation combinations of tramadol and acetaminophen." (Pl.'s Opp'n Br. p. 47.) Even if true, this fact is immaterial.[43]

[43] Besides being immaterial to the inquiry at hand, Ortho-McNeil's allegation is not supported by the prior art. As Ortho-McNeil points out, the WHO Guidelines and Sorge reference teach co-administering a peripheral analgesic with a weak opioid while titrating, i.e., incrementally increasing, the dose of the weak opioid in a three-step individualized treatment regimen tailored to the pain needs of a specific patient. (OMP Facts ¶¶ 70, 74-75.) Therefore, Ortho-McNeil argues, the WHO Guidelines' three-step regimen, also taught by Beyer, Senn, Brinkmann, and Meier is inconsistent with using a composition containing a fixed ratio of tramadol and acetaminophen.

To the contrary, Sorge and Brinkmann teach that such fixed ratio compositions can be used in the three-step regimen. Sorge states that if codeine is used as the weak opioid (as opposed to tramadol), "an entire series of preparations [are] available that contain a fixed combination of codeine with a peripheral analgesic," that could be used. (Brown Decl., Ex. 17, at TR00007-08.) Ortho-McNeil ignores this teaching. Additionally, Ortho-McNeil fails to explain the Brinkmann reference's statement that it is an "oncological disadvantage . . . that there are few fixed combinations of analgesics on the market . . . [because they] can facilitate a reduction of the individual dosage of the components and thus reduce the risk considerably." (Id. ex. 18, at TR000043.) Brinkmann then recommends the co-administration of individual analgesics as a "way to get around" this disadvantage. (Id.)

These explicit teachings are simply not consistent with an allegation that these references teach away from "fixed ratio, single formulation combinations of tramadol and acetaminophen." (Pl.'s Opp'n Br. 47.) No rational fact finder could agree with Ortho-McNeil's selective reading of the prior art. The prior art must be judged for what it teaches as a whole. See, e.g., Ormco Corp., 463 F.3d at 1307-08.

Essentially, this is an argument that the above references teach away from the "pharmaceutical composition" limitation, not the "about 1:5" limitation, and thus, the argument is unavailing. Again, it is not necessary for Kali to identify a suggestion or motivation to create a tramadol/acetaminophen mixture contained in a pharmaceutical composition. Flick already describes these limitations together, and therefore, there are no prior art references that need to be modified or combined to achieve them. The issue is whether there is a motivation to modify Flick, or combine Flick with other prior art to achieve the "about 1:5" weight ratio.

Finally, Ortho-McNeil argues that Sorge, and the other references that employ the WHO Guidelines, teach away from administering tramadol and acetaminophen at a 1:5 weight ratio, and towards using a 1:20 weight ratio. Ortho-McNeil points out that Sorge and the WHO Guidelines teach to titrate the weak opioid while following the three-step ladder regimen. As Ortho-McNeil explains, this means that while co-administering a combination of a peripherally acting analgesic and a weak opioid one would keep the non-opioid dose stable, and would "start with a low daily dose [of the weak opioid], using small doses and a low frequency of administration, and gradually increase the dose and frequency

over the course of days until the desired degree of pain relief is achieved." (OMP Facts ¶ 75 (citing Brown Decl., Ex. 19 (Beyer), at TR000057 ("The adjustment phase when using opioids can last 1-2 weeks since it is recommended that the optimum dosage be approached from a low level."); see also id. ¶ 85.). Following this teaching, and the doses disclosed in Sorge, Beyer, and Senn, Ortho-McNeil asserts that the person of ordinary skill would start by combining the lowest suggested dose of tramadol, 50 mg, with either 500 mg or 1000 mg of acetaminophen, and thus would use a weight ratio of either 1:10 (50mg/500mg) or 1:20 (50mg/1000mg), not 1:5. (OMP Facts ¶¶ 85-86 (citing Stanski Val. Rep. ¶¶ 23-24, 29, 53-54, 65-66, 68).) The person of ordinary skill allegedly would then slowly increase the tramadol dose until sufficient pain relief was achieved. (OMP Facts ¶ 85; Stanski Val. Rep ¶ 65.)

Kali does not dispute Ortho-McNeil's claims about the prior art's titration teachings. But the Court finds that no reasonable fact finder could conclude these suggestions teach away from either modifying Flick, or combining it with other prior art, to achieve "about 1:5." First, while applying the titration teaching to the suggested doses of Sorge, Beyer, or Senn may suggest *starting* with a weight ratio

of either 1:10 or 1:20, those teachings also plainly suggest subsequently using ratios that move *toward* "about 1:5." As Ortho-McNeil and Dr. Stanski urge, the prior art teaches the person of ordinary skill to *increase* the dosage of tramadol until sufficient pain relief is achieved. (OMP Facts ¶ 85; Stanski Val. Rep. ¶ 65.) The upshot of this teaching is that the tramadol dose may continue to be increased throughout its entire suggested dosage range if necessary to achieve sufficient pain relief. Neither Ortho-McNeil nor its experts allege that the person of ordinary skill would stop titrating the tramadol dose before reaching its maximum dose. Thus, using the suggested doses in Sorge, Beyer, and Senn, one of ordinary skill would start by co-administering 50mg of tramadol with either 500 or 1000 mg of acetaminophen (1:10 / 1:20), and incrementally increase the tramadol until reaching 100 mg, and a weight ratio of either 1:5 or 1:10. As a result, the titration teaching fails to teach away from "about 1:5." Indeed, it teaches toward it.

Second, while Ortho-McNeil focuses on the titration teaching's ramifications for the Sorge, Beyer, and Senn doses, it fails to recognize what that teaching means for the remaining prior art, namely, the Meier reference and the Flick patent. When Meier's minimum tramadol dose of 100 mg is titrated up to its

maximum dose of 200 mg against a dose of 500 mg of acetaminophen, the weight ratios taught are 1:5 to 1:2.5. If the person of ordinary skill chose to use 1000 mg of acetaminophen instead, the weight ratios taught are 1:10 to 1:5. Neither option would motivate one to avoid the "about 1:5" range. The titration teaching also fails to teach away from "about 1:5" to the person of ordinary skill in the art who was looking, not to combine Flick with other prior art to achieve the claimed ratios, but to modify Flick alone. Indeed, the titration teachings seem to provide an independent suggestion or motivation to modify Flick's 1:10 to "about 1:5," apart from the presumption that the person of ordinary skill would routinely experiment to find an optimum weight ratio. Flick's example 23 describes a tablet containing 25 mg of tramadol and 250 mg of acetaminophen. Increasing the tramadol dose while keeping the acetaminophen dose stable moves the weight ratio from 1:10 toward 1:5. Furthermore, as explained in the Court's anticipation analysis, the Flick patent itself teaches that the next highest (and preferred) oral dose of tramadol that could be used is 50 mg. '589 patent, col. 12, l. 25. Additionally, Sorge, Beyer, and Senn all teach that 50 mg is the lowest amount of tramadol that should first be used. When 50 mg of tramadol is combined with 250

mg of acetaminophen, this creates a tablet with a weight ratio of exactly 1:5. At the very least, no reasonable person could find that the titration teaching would cause someone to modify Flick *away* from "about 1:5." Ortho-McNeil has failed to point to evidence that could cause a reasonable fact finder to conclude that the prior art teaches away from "about 1:5."

**f. Other Secondary Considerations**

Aside from unexpected results, Ortho-McNeil claims that other objective indicia of the nonobviousness of Claim 6 exist. When present, such secondary considerations must be considered by the Court. Ruiz v. A.B. Chance Co., 234 F.3d 654, 667 (Fed. Cir. 2000). "Evidence of secondary considerations . . . are but a part of the 'totality of the evidence' that is used to reach the ultimate conclusion of obviousness." Richardson-Vicks, 122 F.3d at 1483 (citation omitted). While "secondary considerations may often be the most probative and cogent evidence in the record," Stratoflex, 713 F.2d at 1538, and "may be sufficient to overcome a prima facie case of obviousness," In re Beattie, 974 F.2d 1309, 1313 (Fed. Cir. 1992), it is also true that "they do not control the obviousness conclusion," Newell Cos., Inc. v. Kenney Mfg. Co., 864 F.2d 757, 768 (Fed Cir. 1988). Ortho-McNeil

alleges that the record contains evidence of four additional secondary considerations: commercial success, long felt but unsolved need, copying, and skepticism.

First, as to commercial success, Ortho-McNeil cites the expert report of Dr. Richard Rozek, who claims that Ultracet has achieved significant commercial success due to its product characteristics, as opposed to pricing or marketing strategies. (Rozek Rep. ¶ 7.) Dr. Rozek also points out that Ultracet's sales are in the top 10 percent of its market despite competing against cheaper products. (Id. ¶ 21.)

Second, Ortho-McNeil cites numerous expert reports attesting that Ultracet met a long felt, but unsolved need in the industry for an effective analgesic to treat moderate to moderately severe acute and chronic pain without causing the adverse side effects of tramadol or other comparable analgesics. (See Gudin Rep., ¶¶ 4-10; Bennett Rep., ¶¶ 2-7; Zun Rep., ¶¶ 11-23; McKeever Rep., ¶¶ 10-13.)

Third, as evidence of copying, Ortho-McNeil points to Kali's ANDA filing, in which Kali seeks permission from the FDA to market a generic version of Ultracet.

Fourth, and finally, Ortho-McNeil presents evidence of scepticism by doctors who claim they were initially doubtful that Ultracet would be effective given that it contained 25 percent less tramadol than Ultram, Ortho-McNeil's tramadol-only product. Additionally, these doctors doubted whether Ultracet had any value, given the wide availability of generic versions of individually formulated tramadol and acetaminophen products. (Gudin Rep., ¶¶ 13-16; Bennett Rep., ¶¶ 20-24; McKeever Rep.., ¶¶ 14-16; Zun Rep., ¶ 25.)

Kali responds that the evidence is immaterial because it pertains to features of Ultracet and its 1:8.67 weight ratio, and thus is not probative of the alleged nonobviousness of Claim 6. The Court agrees. As explained above with regard to unexpected results, "[a] nexus between the merits of the claimed invention and the evidence of secondary considerations is required in order for the evidence to be given substantial weight in an obviousness decision." Simmons Fastener Corp. v. Illinois Tool Works, Inc., 739 F.2d 1573, 1575 (Fed. Cir. 1984) (citing Stratoflex, 713 F.2d at 1539); see also Ormco, 463 F.3d at 1311-12 ("Evidence of commercial success, or other secondary considerations, is only significant if there is a nexus between the claimed invention and the commercial success."); Brown &

Williamson Tobacco Corp. v. Philip Morris, Inc., 229 F.3d 1120, 1130 (Fed. Cir. 2000) (explaining that "if the marketed product embodies the claimed features, and is coextensive with them, then a nexus [between the product and commercial success] is presumed and the burden shifts to the party asserting obviousness to present evidence to rebut the presumed nexus").

Here, Ultracet's 1:8.67 weight ratio lies outside the scope of Claim 6's 1:3.6 to 1:7.1, i.e., "about 1:5," range. Thus, there is no nexus between Ortho-McNeil's objective evidence of nonobviousness and "the merits of the claimed invention." Such a nexus would be necessary for this Court to give that evidence substantial weight in its obviousness decision. See Simmons, 739 F.2d at 1575 (emphasis added).

In conclusion, the Court finds that a reasonable fact finder would conclude that Ortho-McNeil has failed to rebut Kali's prima facie case of obviousness. Thus, on the record before the Court, Kali has "prove[n] by clear and convincing evidence that [the] claim that is challenged cannot reasonably be held to be non-obvious." See Knoll Pharm., 367 F.3d at 1383. Accordingly, the Court will grant Kali summary judgment of invalidity of Claim 6 of the '691 patent on the grounds

of obviousness.

**4. Public Use Bar**

The final ground for invalidity asserted by Kali is the public-use bar. Under 35 U.S.C. § 102(b), an invention is unpatentable if it was "in public use . . . in this country, more than one year prior to the date of the application for patent in the United States." It is undisputed that the critical date here is September 6, 1990. Whether a patent is invalid under the public-use bar is a question of law based on underlying facts. See U.S. Envtl. Prods., Inc. v. Westall, 911 F.2d 713, 715 (Fed. Cir. 1990).

Kali points to a May 4, 1990 clinical trial Ortho-McNeil performed in order to test "the efficacy and safety of the oral combination of tramadol with acetaminophen relative to its components and placebo in patients with pain following surgery" (Minn Decl., Ex. A, at POMP5292.), as the allegedly invalidating public use. However, Kali does not contest that the participating patients in this clinical trial were administered separate capsules containing either tramadol or acetaminophen. It is undisputed that the clinical trial did not involve capsules containing both tramadol and acetaminophen. (Pl.'s St. Undisputed Mat.

Facts ¶ 18; Def.'s Supp. St. Undisputed Mat. Facts, at p. 1.) "When the asserted basis of invalidity is prior public use, the party with the burden of proof must show that 'the subject of the barring activity met each of the limitations of the claim, and thus was an embodiment of the claimed invention.'" Juicy Whip, Inc. v. Orange Bang, Inc., 292 F.3d 728, 737 (Fed. Cir. 2002) (quoting Scaltech Inc. v. Retec/Tetra, L.L.C., 178 F.3d 1378, 1383 (Fed. Cir. 1999)). As the Court concluded above, the "pharmaceutical composition" limitation of Claim 6 requires a medicinal preparation comprising an intimate admixture, prepared outside the body, generally in the form of a dosage unit, such as a tablet or capsule. Claim 6 requires this pharmaceutical composition to be comprised of both tramadol and acetaminophen. Thus, regardless of whether Ortho-McNeil's clinical trial was a public use, it did not involve the claimed invention. Accordingly, Kali's motion for summary judgment of invalidity on the basis of the public use bar will be denied.

## IV. Conclusion

The Court concludes that, as a matter of law, Kali has not infringed Claim 6, formerly of the '691 patent, and now of the RE221 patent. The Court further

concludes that Teva/Barr have, as a matter of law, infringed Claim 6 of the RE221 patent. Additionally, the Court concludes as a matter of law that Claim 6 of the RE221 patent is not invalid for indefiniteness, or under the public use bar; however, Claim 6 is invalid for anticipation and for obviousness. Defendants' motions for summary judgment will be denied or granted accordingly. ____

/s/ John C. Lifland, U.S.D.J.

**April 4, 2007**_____